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Preventing blindness from glaucoma

Better screening with existing tests should be the priority

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The detection and management of primary open angle glaucoma is a major healthcare issue. It is the second largest cause of blindness in the world and affects some 66.8 million people, leaving 6.7 million with bilateral blindness.[1] In the United Kingdom, the ageing of the population means that the number of cases is expected to increase by 30% in the next 20 years.[2]

In primary open angle glaucoma, the retinal ganglion cells—the nerves that carry the visual stimulus from the retina to the brain—undergo apoptosis after insult at the head of the optic nerve. The progressive loss of ganglion cells leads to characteristic structural changes at the head of the optic nerve and functional loss to the visual field. Glaucoma is often, but not necessarily, associated with raised intraocular pressure. A paper in this week's *BMJ* shows that, in general, treatment to reduce intraocular pressure leads to delayed progression of visual field loss in patients with manifest open angle glaucoma.[3] More research is needed in the subgroup of patients without increased intraocular pressure, to determine which patients with normal tension glaucoma will benefit most, since this meta-analysis was unable to show a consistent benefit in these patients.[3] In 1982 Grant and Burke wrote a paper intriguingly titled "Why do some people go blind from glaucoma?"[4] From a sample based in the United States, they found that some 30% of people who go blind from this disease are blind, in both eyes, at presentation. Most of the blind patients were aware of their decreasing vision for months, or even years, before they sought medical advice. Blindness was defined as an acuity of less than 20/200 (< 6/60 metric Snellen) in the better eye, or a residual visual field of less than 10 degrees. In a more recent report by Sinclair,[5] who investigated registrations for blindness due to glaucoma in Fife between 1990 and 1999, a considerable number of patients were found to have moderate to advanced visual field loss at their first appointment, with 23% being eligible for registration as blind.

We recently reviewed all referrals for glaucoma and registrations for blindness or partial sight at Manchester Royal Eye Hospital during 2003. We found that 28% of patients with glaucoma were registered blind within three years of first presentation and that relatively few of those with blindness or partial sight were referred initially by optometrists: 42% compared with 90% nationally for all people with suspected glaucoma (unpublished data).This indicates that there may be barriers to access, such as the perceived costs associated with getting an eye examination. Laidlaw has already shown that the imposition of fees for sight tests had a negative effect on the number of referrals to Bristol Eye Hospital for glaucoma.[6] New technologies, such as optic nerve and nerve fibre layer imaging devices, are promoted on the basis of being able to detect glaucoma before the patient has a reproducible visual field defect (because, unsurprisingly, those with more rapidly progressing disease leading to blindness are more likely to present with marked visual field loss[7 8]). But new technologies are not required to detect the extensive visual field loss that many of those who progress to blindness have at first presentation: the tests we already have are capable enough if used appropriately.

A series of epidemiological studies has shown that the more widespread use of existing technologies will improve early detection. In the north London trial,[9] 75% of cases with "definite" glaucoma were new cases, and these were detected with a simple combination of tests—suprathreshold perimetry, tonometry, and slit lamp examination of the anterior eye and optic nerve head—that are readily available at most optometric practices.

The problem is not lack of suitably sensitive technologies but the infrequent use of existing technologies. Breaking down barriers to access, targeted screening, and a campaign to inform patients about the importance of regular eye examinations might have much more effect on the number of patients going blind from this disease than the current concentration of effort into the development of more sensitive technologies.

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Investigation of recurrent miscarriages

A successful pregnancy is the most likely outcome

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Human reproduction is hopelessly inefficient. The maximum probability of conceiving during a menstrual cycle is only about 40%. One third of conceptions do not result in the delivery of a baby.[1-3] But this inefficient process produces astoundingly good outcomes. The vast majority of continuing pregnancies result in the birth of a healthy human being who will, eventually, pass his or her genes on to the next generation. Miscarriages—clinically detectable pregnancies that fail to progress—are the inevitable byproduct of such a process. They are common and often remain unexplained, even after investigation. They are a source of distress for women and their partners. When a woman has had two or more miscarriages, she is likely to seek professional help, in the hope that a cause and a cure will be found.

Because 10-15% of clinically recognised pregnancies end in miscarriage, and because most women who have one, two, or even three first trimester miscarriages will nevertheless go on to have a successful pregnancy, investigations are usually done only when a woman has recurrent miscarriages.[4 5] The United Kingdom's Royal College of Obstetricians and Gynaecologists, which defines recurrent miscarriage as the loss of three or more pregnancies, and the American College of Obstetricians and Gynecologists, have both published similar guidelines on the management of recurrent miscarriage.[6 7] Recurrent miscarriages have a range of possible causes including genetic, anatomical, endocrine, immune, infective, thrombophilic, and unexplained.

Balanced chromosome translocations, in which sections of chromosomes change their geographical position on the chromosomal map without any loss or gain of important genetic material, are an important cause of recurrent miscarriages because they are common; one in 500 people carries a balanced translocation. When one member of a couple carries a balanced chromosome translocation, the risk of having a miscarriage is approximately doubled. In 3-5% of couples with recurrent miscarriage, one partner has a balanced translocation. Peripheral blood karyotyping of both partners is considered a mandatory investigation of couples with recurrent miscarriage but, in this week's *BMJ*, Franssen et al raise the question of whether other factors, such as family history of miscarriages, should be taken into consideration when deciding who should be karyotyped.[8] When a balanced translocation is identified, it is useful to karyotype miscarriage products to see if they are the result of unbalanced translocations.

Congenital abnormalities of the uterus probably account for some recurrent miscarriages, but the extent of their contribution is uncertain. The guidelines from the Royal College of Obstetricians and Gynaecologists recommend an ultrasound scan of the pelvis for women with recurrent miscarriage, but this recommendation is based solely on the clinical experience of the guideline development group, rather than on published evidence. Some centres use hysterosonography (ultrasound with the introduction of an echocontract fluid into the uterus).[6]

It is traditional to screen for maternal endocrine disease in the investigation of recurrent miscarriage. But the prevalence of these conditions is no greater in women who miscarry than in the general population, so screening is not worth while.[6]

Antiphospholipid syndrome, in which anticardiolipin antibodies and lupus anticoagulant are present, is detectable in 15% of women with recurrent miscarriage. Its identification is important, because treatment with aspirin or heparin or both significantly improves the likelihood of a live birth.[9] But a recent review of the management of the obstetric antiphospholipid syndrome recommended that healthy women with fewer than three early miscarriages should not be tested or treated for antiphospholipid syndrome because, for these women, there is no evidence that drug treatment during pregnancy is beneficial.[10]

Infections with bacteria, viruses, and other organisms such as toxoplasma and listeria can all interfere with pregnancy, but none seems to be significant causes of recurrent early miscarriage. The Royal College, on the basis of evidence obtained from experts but not from randomised controlled trials, recommends that TORCH screening for infection (looking for toxoplasma, other viruses, rubella, cytomegalovirus, herpesvirus, and sometimes HIV) should be abandoned in the investigation of recurrent miscarriage.[6]

There is much debate, but little evidence from prospective studies, on the importance of thrombophilic defects, such as Factor V Leiden mutation, in the aetiology of recurrent miscarriage. In the absence of convincing evidence, there is no agreed protocol for investigation of these defects.

With so many possible causes for recurrent miscarriage, it would be tempting to think that the prognosis for those women whose recurrent miscarriages are unexplained (about half) is dire.[7] But three quarters of these women will go on to have a successful pregnancy if offered nothing more, and nothing less, than tender loving care and reassurance through ultrasound that

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