

# **The Early Diagnosis of Visual Defects**

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In July, 1965, the Office of Health Economics held a colloquium on Surveillance and Early Diagnosis in General Practice at Magdalen College, Oxford. It was apparent from the discussion at this meeting that General Practitioners believed that if they were to act effectively in this field, they had to have clear cut information on current screening methods and the impact of early diagnosis of disease on the long term health of the patient. As a result of this view the Advisory Committee set up by the Office of Health Economics came to the conclusion that the best method of furthering this issue was to ask experts in a number of relevant clinical fields to write short papers specifically for General Practitioners. *The Early Diagnosis of Visual Defects* is the second of these papers in the ensuing series.

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THE greatest prevalence of unrecognised defects occurs in the elderly and the young. Usually the defect will occur gradually affecting either the visual acuity of one eye only, or the visual field of one or both eyes.

In the very young, the defect which goes unnoticed until school age and the consequent school medical examination is unilateral suppression amblyopia induced by strabismus or anisometropia. There is a very much better response to treatment if the problem can be detected at about age three when it is possible to assess a child's visual acuity with accuracy. Further there now exist appropriate diagnostic techniques such as the simple 'cover test' which can be efficiently administered by an orthoptic technician to children of this age.

In the elderly, the more important causes of defective vision include vascular disorders, cataract, macular degeneration, diabetic retinopathy and chronic glaucoma. However, only the last two offer scope for early detection and treatment. The detection of diabetic retinopathy depends in turn on the early detection of diabetes.

Chronic glaucoma is an important cause of blindness and signs of the disease may be present for a long while before the patient is conscious of any abnormal symptoms and it is therefore a suitable problem for early detection. Treatment is based entirely on the reduction of intra-ocular pressure. Detection of the disease is frequently by measurement of this pressure by tonometry, but this presents problems in that it is not possible to indicate an upper limit for normal pressure. It also gives a positive finding in many who have normal visual fields and who are unlikely to have future loss of vision. It would be unreasonable to treat these patients in the hope that they might benefit, especially as the treatment has undesirable side effects and interferes with the subjects' enjoyment of life. There is a clear need therefore, for the development of tests which can be used on those with pressures above a certain level and which will predict more accurately the probability of future loss of vision.

Meantime, other methods of early diagnosis, all of which are cheaper than tonometry, include determination of the visual fields, observing the retina by ophthalmoscopy and selection by family history. The first method detects those who already have a significant loss of function and is thus concerned with established disease rather than the true presymptomatic stage. Ophthalmoscopy is practised by every optician in the course of a routine eye test, but the number of false positives is high until a late stage in the disease. There is a high prevalence of abnormality amongst relatives of known sufferers, so this does provide a method of initial selection to be followed by a more thorough examination. It is recommended that this last method be implemented under the direction of the General Practitioner.

**PROBLEMS AMONGST THE YOUNG AND THE OLD**

**ALTHOUGH** many visual defects, affecting as they do the most important and informative of the special senses, tend to attract the notice of the sufferer at an early stage, this is not invariably so. The defect for which early advice is sought tends to be one of relatively rapid onset, affecting the central vision of both eyes, and occurring in a patient who is both mentally alert and able to communicate his symptoms. It follows that one would expect to find the greatest prevalence of unrecognised defects in the elderly and the very young, and that they would be of gradual onset affecting either the visual acuity of one eye only, or the visual field of either one or both eyes. It is in these groups that unrecognised disease should be actively sought.

In the very young, the commonest unsuspected defect is unilateral suppression amblyopia induced by strabismus (which may be slight or intermittent and so pass unnoticed) or anisometropia (inequality in refractive error). Both present an opportunity for early detection and will be discussed later.

At the other end of the life-span, the incidence of visual defects rises steeply with age. In the elderly, the more important causes of defective vision include vascular disorders such as occlusion of retinal arteries or veins; cataract; the so called 'senile' macular degenerations; diabetic retinopathy; and chronic glaucoma. Of these, only diabetes and glaucoma at the present time offer scope for early detection and treatment. Vascular disorders are usually sudden in onset, and any detection and prevention would have to be considered against the wider background of vascular disease in general. Cataract is treatable only by the crude though effective method of removing a lens which has become more of a liability than an asset. We are as yet ignorant of its aetiology and powerless to influence its progress, so that its discovery before the patient complains of its effects serves no useful purpose whatever. The macular degenerations, unhappily, are ill understood. Some are probably related to vascular disease, and others may well be determined genetically despite their late manifestations. Our lack of knowledge about these prevalent and distressing disorders makes rational therapy non-existent and early detection pointless. As a group they form the largest single cause of irreversible blindness in the elderly.

Diabetic retinopathy makes a significant contribution to the numbers of registered blind. The figures for 1962 reported 825 newly-registered blind persons due to diabetes out of a total of newly-registered blind of just over 11,500. There is some doubt as to whether this figure is disproportionately great since the diabetic may well, by his better contact with the social and medical services, stand a significantly better chance of detection and registration as a blind person than, say, the elderly patient with macular degeneration. It is reasonable to suppose that early detection and treatment may delay, if not prevent, the development of retinopathy, and hence that screening for diabetes may prevent or delay a certain amount of visual defect. Further discussion of the detection of unsuspected diabetes is, of course, outside the scope of this paper.

#### CHRONIC GLAUCOMA

Chronic glaucoma appears at first sight to be a condition ideally suited to early discovery and treatment. It is major cause of blindness—ranking high in the figures for blind registration in the elderly<sup>1</sup>—1400 out of over 11,500 new cases registered in 1962—and because the visual loss does not involve central vision until a late stage, signs of the disease may be present for a long time before the patient notes any symptoms.

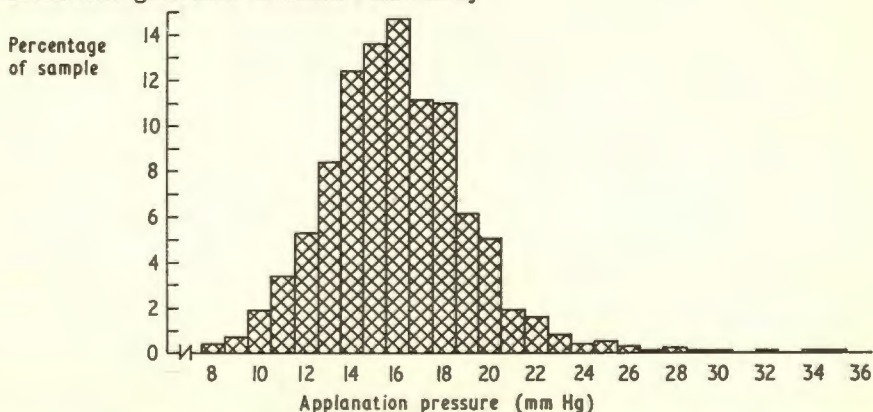
To establish the diagnosis of chronic glaucoma beyond all reasonable doubt, it is necessary to demonstrate the coincidence in one eye of an intra-ocular pressure in excess of that of the 'normal' individual, together with a typical defect in the visual field, preferably accompanied by an optic disc showing the pallor and excavation known as glaucomatous cupping. The raised pressure should be shown to be unaccounted for by any other ocular disease or structural abnormality.

Classically it has been believed that the raised intra-ocular pressure is responsible for the development of the changes in the disc and therefore for the progressive loss of vision, although there has long been a school of thought which rejects this hypothesis either in whole or in part. The treatment of chronic glaucoma is based entirely on reduction of the intra-ocular pressure to 'safe' levels. Recent work by Armaly<sup>2</sup> and Graham and Hollows<sup>3</sup> has shown, however, that the correlation between pressure and field defect is less marked than would be expected if raised pressure were the sole cause of glaucomatous optic atrophy. Thus, although screening for early glaucoma by means of tonometry is attractive because of its initial simplicity an examination of its efficiency as an index of present or impending loss of visual field might well reveal serious objections to the method.

It has long been known that intra-ocular pressure in the population is distributed in a slightly asymmetrical pattern about the mean level, there being a small excess of higher pressures. More recently it has been shown that this excess increases with advancing age, being absent or insignificant in the young in whom pressure may well show a symmetrical normal distribution<sup>4,5</sup>. As in other fields, such as diabetes and hypertension, the distribution (Fig. 1) shows no clear distinction between 'normal' and 'abnormal' pressures, and it is not possible to give an upper limit for normal pressure. Attempts have been made to do this by using the fact that the observed distribution is sufficiently close to a Gaussian curve for probabilities to be calculated for any given level of pressure by standard statistical methods. If intra-ocular pressure shows a 'normal' distribution, individuals with pressures of over two standard deviations from the mean value are so infrequent in occurrence that they may reasonably be considered as having abnormal pressures. Unfortunately, however, pressure is *not* so distributed, and it is improper to consider those who fall outside a symmetrical distribution as pathological unless other evidence is available to distinguish them from those whose pressure lies within the normal curve. At present no convincing evidence of this has been produced, and unless this is forthcoming,

**Figure 1**

Actual findings in 1963 Rhondda Fach survey



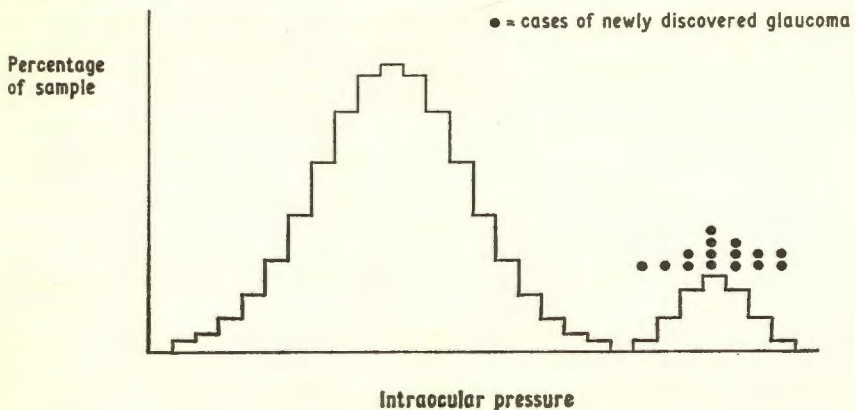
these individuals can be regarded as abnormal only in a strictly limited statistical sense which may have little prognostic significance.

#### CAN A UNIVERSAL ABNORMAL LEVEL OF INTRA-OCULAR PRESSURE BE DISTINGUISHED IN SCREENING FOR CHRONIC GLAUCOMA?

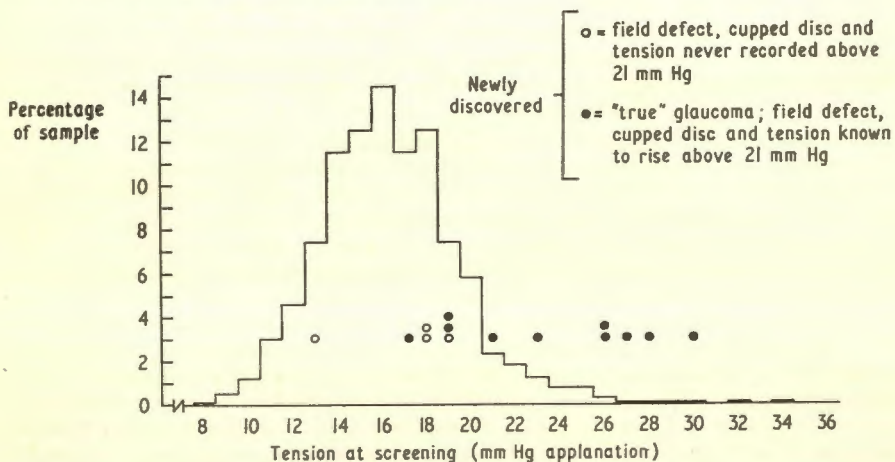
Ideally, if one were to use tonometry as an initial screening test for chronic glaucoma, one would like to see a bimodal type of distribution clearly separating 'normal' from 'abnormal' pressures, with defects in the visual field confined to the 'abnormal' portion (Fig. 2). The actual findings in this respect are disappointing (Fig. 3). Not only is there a smooth transition from the main body of the population to those with higher pressures, but marked glaucoma-like defects in the visual field occur at pressures which would not be regarded as 'abnormal' even on the basis of an upper limit of two standard deviations above the mean value. This means that false negatives occur with undesirable frequency when a single measurement of pressure is used. Follow-up studies by Graham and Hollows<sup>3</sup> have shown that some of these patients do at times have pressures above 'normal', so that they are false negatives for the fully developed disease with 'raised' pressure, field defect and cupped optic disc. Others, however, have never shown higher pressures, and appear to have developed the typical disc and field changes of chronic glaucoma at 'normal' levels of pressure. When one also considers the fact that it has been found that there is no apparent correlation between intra-ocular pressure and the type of field defect usually



**Figure 2**  
 'Ideal' distribution of pressure and relation to established glaucoma



**Figure 3**  
 Intra-ocular pressure in 1920 male right eyes



considered to be the earliest sign of glaucomatous optic atrophy<sup>2</sup>, it becomes clear that we have yet much to learn about the aetiology and early natural history of this disease.

It has been suggested that the rise in pressure precedes the development of loss of visual field by about fifteen years. This suggestion is based on the fact that the point at which the age incidence curves for raised pressure and fully developed glaucoma start to rise, are separated by this interval. This theory, although not disproven, does not emphasise the considerable discrepancy between the overall prevalences of raised pressure and full glaucoma. In one survey where both were measured in a defined population (most surveys reported are 'case finding' in nature, the composition of the population being unknown, and the prevalence figures therefore unreliable) there were 397 patients with pressures of 21 or more and only 14 patients with fully developed glaucoma. Further, it can be shown, using the prevalence figures and ages from the same survey, that of 1000 subjects aged 40, a total of 29,310 years of life would be expected, and of these, there would be 2838 years lived in a state of asymptomatic ocular pressure over 21 mm. Hg., and only 152 years in a state of chronic glaucoma (not, be it noted, blindness from this disease, but simply presence of field defect). This is a ratio of seventeen years of asymptomatic ocular hypertension for every year of glaucoma, a ratio which scarcely justifies preventive treatment of the asymptomatic condition. The true ratio is in fact less favourable still and a more full discussion is published elsewhere<sup>3</sup>. These figures suggest that by no means all patients with 'raised' pressure are destined to develop loss of visual field, and unless they are to progress to full glaucoma they will not benefit from the discovery of their ocular hypertension. There is a clear need, therefore, for a test or tests which can be used on those with pressures above a certain level, in order to predict more accurately the probability of future loss of visual field. In the past much energy has been expended on tests based on measurement of pressure or of the resistance of the aqueous outflow system (which is the main factor in determining pressure) under various conditions of stress. A detailed account of all these tests would be out of place in the present paper. It will be sufficient to say that, although some of the techniques may give information about the future behaviour of ocular pressure in the subject concerned, none has been proven to be an accurate predictor of future loss of field. Since all these tests are closely related to pressure and its variation, and the correlation between pressure and field defect is by no means absolute, most of the objections to pressure as an index of field loss apply to these more sophisticated tests.

To summarise the position of tonometry as a screening test, it can be shown that it will fail to indicate a significant number who suffer from glaucoma, and will produce a large number of subjects who are asymptomatic, have normal visual fields and are distinguished from the rest of the population only by the fact that their pressure is statistically rather high, and possibly by statistically abnormal results from various supplementary tests dependent on measurement of pressure or outflow under stress.

The number of these subjects makes it improbable that the majority are destined to show detectable loss of vision from glaucoma. It would be undesirable to attempt treatment of these subjects as a preventive measure, especially as the treatment itself has undesirable side effects and interferes with the subjects' enjoyment of life. A trial of such treatment by the author has shown that intensive and close supervision, such as might well induce unnecessary alarm and despondency, is necessary to persuade the majority of asymptomatic patients to continue therapy for more than a short time. It seems clear that until a test has been devised which gives a reasonable indication of the probability of future visual impairment in the patient with asymptomatic ocular hypertension, tonometric screening leaves a great deal to be desired. Even if such tests pass their present experimental stage, the method will still have the disadvantage that a single measurement of pressure may fail to detect a patient who has already suffered some visual loss.

#### OTHER TECHNIQUES FOR CHRONIC GLAUCOMA SCREENING

In view of these objections to the method hitherto most commonly used, one must consider what other possible indices could be employed for initial selection. There are in fact three possibilities, namely screening of the visual field, screening by ophthalmoscopy and selection by family history. These will now be considered in turn.

The normal methods of clinical investigation of the visual field are unsuitable for use in screening, being too tedious and requiring considerable training. There are, however, several devices which can be used to make a rapid assessment of the visual field under reasonably standard conditions<sup>6,7</sup>. These instruments depend upon the serial presentation of predetermined stimuli, either singly or in groups. The stimuli may be distributed evenly over the whole field, or, to increase sensitivity for a particular disease, grouped selectively in the areas of greater diagnostic importance for the condition under investigation. The instruments can be made reasonably portable, and the examination, although longer and requiring more co-operation than tonometry, can be effectively administered to large numbers by a technician who refers all those with defective performance for further examination by an ophthalmologist.

This method of screening selects those who already have significant loss of function, eliminating the unsatisfactory 'presymptomatic' group found in tonometry. It is possible if the test is not sufficiently sensitive to miss small defects in the visual field, but this can be rectified by increasing sensitivity, albeit at the cost of reduced speed. By its nature the method detects unsuspected but established disease rather than a true presymptomatic state, but in our present state of ignorance about the influence of factors other than intra-ocular pressure on the development of glaucoma this is an advantage, not, as sometimes claimed, a defect. The main disadvantages are that the subjects must be reasonably intelligent and co-operative, and that a positive result

requiring investigation is frequently produced by other, often trivial ocular defects, the visual field on both perimeter and scotometer being normal. Finally, if, in an attempt to eliminate all false negatives sensitivity is raised to too high a level it is possible to detect very minor defects whose value as indices of future significant visual loss is at present difficult to assess.

Screening for glaucoma by ophthalmoscopy is in fact the oldest method and one which, consciously or unconsciously, every ophthalmologist and optician practises in the course of a routine eye test. Unfortunately the glaucomatous optic disc is not unequivocally abnormal except at an undesirably late stage in the disease. Before this is reached, the disc shows an enlarged and usually sharply defined central depression or 'cup' with a tendency for the vessels to shift towards the nasal side. This appearance is not clearly distinguishable from the large so-called 'physiological' cup shown by many perfectly normal discs. As a result, the rate of false positives is bound to be high, since most of the referrals will be found to have large physiological cups with normal visual fields. The occurrence of false negatives is also possible, the frequency depending on the sensitivity of the visual field examination. In one trial with a field-screening device no patient with a field defect detectable by the screening device had been passed as 'normal' by the ophthalmocopist<sup>8</sup>. It might be expected from this result that ophthalmoscopy in experienced hands can be of the same order of efficiency as field screening, detecting those with more than minor field defects with a high false positive rate.

The final method of detection depends upon the fact that it is possible to show a high prevalence of abnormality among the relatives of known sufferers. This has been shown both for pressure<sup>8,9</sup> and for fully-developed glaucoma<sup>10</sup> where the familial incidence has been put as high as 38 per cent.

Initial selection by family history allows a more thorough examination instead of a simple screening test, and could enable better use to be made of limited facilities.

#### THE COST OF SCREENING FOR CHRONIC GLAUCOMA

All the screening procedures described are quick and reasonably simple. They have proved acceptable in practice, and although in tonometry there is a theoretical risk of corneal damage, experience in many thousands of measurements has shown that the risk is very small indeed. Field and ophthalmoscopic screening are naturally entirely free from risk, being purely subjective in nature.

As resources are likely to be limited in the foreseeable future the question of relative cost, often ignored, is of considerable importance. As none of the methods discussed involves any large expenditure on materials, it is possible to make a reasonable comparison on the basis of time spent per new case detected. This was attempted by the author, using figures from his own and other surveys<sup>11</sup>. The results in the detection of unsuspected field defects are shown (Table A) for a team of ophthal-

**Table A**

Relative times spent in detecting Glaucomatous Field Defects

	<i>Hours per case detected</i>	
	<i>Ophthalmologist</i>	<i>Technician and Secretary</i>
Tonometric Screening	11	71
Field Screening	5	45
Family Study	5	10

mologist, technician and secretary. Tonometry emerges as clearly the most expensive, if the normal routine of investigation recommended for suspects is followed. The more favourable ratios for field screener and ophthalmoscopy are accounted for in large measure by the simpler nature of the subsequent investigation required. The cost per case detected by tonometry can be reduced if the test is used simply as an indication that the subject requires a visual field test, but it has already been pointed out that a single measurement of intra-ocular pressure is an unsatisfactory index for possible field loss.

Even more important is the problem of providing adequate long-term supervision of suspects. In relation to tonometric screening the problem is a formidable one, for about 8 per cent of the population between 40 and 75 years have pressures which, according to many authors, require long-term supervision. Applied to the population of England and Wales, this could result in the unloading of up to 1,600,000 patients on the Hospital Eye Service. Those familiar with the already over-burdened clinics will realise the chaos which would ensue. At the present time the available evidence suggests that expansion of facilities, were this possible, to cope with such an influx is scarcely justified by our limited knowledge of the precise significance of ocular hypertension with normal visual fields.

In the case of field screening and ophthalmoscopy, the problem is less difficult, for it is unreasonable to deny the desirability of supervising the patient with a definite field defect. The process of eliminating false positives in most cases involves only a single examination, and the number of new cases remaining for long-term surveillance is small, only about 0.3 per cent for the age group 40-75 or about 60,000 for England and Wales. This is clearly more within the bounds of possibility, provided that the initial investigation of suspects can be managed. Similar considerations apply to the technique of tracing and examining relatives of known glaucomas.

No consideration has been given in the above review of costs and facilities to the problem of repeat screening. Desirable time intervals for this have not been established for any of the techniques, but there is no doubt that re-examination of previous

'normals' would be required. The rate at which this would add to the numbers requiring long-term supervision would depend on the adequacy of the initial coverage. If this was poor, a more gradual build up to the levels suggested above might be expected.

When all the factors discussed so far are taken into consideration, it would seem that at the present time the most rewarding technique for early diagnosis of glaucoma would be the establishment of a system whereby the relatives of each chronic glaucoma patient under treatment were traced and encouraged, so far as possible, to submit to a brief check consisting of tonometry, field screening and ophthalmoscopy. If at all possible, this should not be carried out in the normal out-patient clinic, for these clinics are already overloaded. Many hospitals already segregate their glaucoma patients into separate clinics, for the disease lends itself to surveillance at specially organised sessions. This tendency should be encouraged and in the planning of such clinics provision should be made for the examination of suspects as well as established cases. What must be discouraged is enthusiastic screening by general practitioner or public health department without adequate backing by the hospital service. So long as this type of activity is confined to isolated surveys, as has been the case so far, it is usually possible to absorb the influx of suspects by utilising the services (often spare-time) of an enthusiastic ophthalmologist, often at the nearest teaching hospital. It would be a mistake to imagine that because this can be and has been done, the Hospital Eye Service as a whole would at present be capable of undertaking the extra work.

#### AMBLYOPIA AMONGST THE YOUNG

At the other end of the life-span, unocular visual defects frequently pass unnoticed until the child reaches school-age and is subjected to the usual school medical examination. It has been known for many years that amblyopia, due to either marked inequality of refraction or to strabismus, responds very much better to treatment in the younger child. A full discussion of this type of amblyopia can be found in textbooks of orthoptics. It is sufficient here to say that the prognosis for restoration of normal vision becomes less favourable with increasing age in the case of inequality of refraction (anisometropia) and with the interval between onset and inception of treatment in the amblyopia of strabismus.

The value of occlusion therapy in the treatment of these types of unocular amblyopia has been amply demonstrated, and it is highly probable that much of the defective vision due to this cause, commonly seen in, for example, recruits for military service, could be cured or greatly improved if detected earlier than is usually the case. Unfortunately, the maximum incidence of convergent squint with amblyopia lies in the age group 2-3 years at a time when the child has passed from the supervision of the infant welfare clinics and has not yet come under the school medical service. Small,

and even gross squints are often overlooked by parents or are noted without their possible implications being realised, while the child with anisometropia is left to ignore or suppress the image in the more ametropic eye. By the time the child reaches his first school medical examination the optimum time for treatment is long past and the results are less satisfactory than they would probably be with earlier detection. In one survey by Sutcliffe<sup>12</sup> a group of 310 3-year-old children showed a prevalence of 3.5 per cent with vision in one eye of 6/60 or less and 5.5 per cent with 6/18 or less. This can be contrasted with 0.6 per cent 6/60 or less and 2.7 per cent 6/18 or less in a group of school leavers, who have been subject only to the present process of selection.

Modern orthoptic techniques have made it possible to obtain reasonably accurate estimates of visual acuity in children from the age of three years upwards, and the presence of latent or manifest squint is easily detected by the simple 'cover test' which is still the basic diagnostic technique in orthoptics. Neither of these tests requires any medication, nor do they in any way distress the average child. A certain amount of skill and training is required to administer the tests effectively, but it is not necessary for the initial examiner to be medically qualified.

It would seem, therefore, that there is a good case to be made out for a trial of visual screening at the age of 3-3½ years. For those detected at such a survey there is a treatment which can effect at best a permanent restoration of normal acuity and in almost all cases a substantial permanent improvement. Bearing in mind that the condition occurs in the very young, while chronic glaucoma is a disease of old age, the potential benefits are probably at least as great as those of screening for the latter. The case for screening is not conclusive, however, as the prevalence of unilateral amblyopia is lower in older age groups as a result of present screening at school and possibly of spontaneous improvement. Some careful follow-up studies are still necessary to establish how much benefit would follow from screening in 3-year-olds in relation to the time and therefore the cost involved.

- 1 SORSBY, A. (1966). *Blindness in England and Wales*. London, HMSO.
- 2 ARMALY, M. F. (1962). *Invest. Ophthalm.* **1**, 618.
- 3 GRAHAM, P. A. and HOLLOWES, F. C., in *Glaucoma, Early Detection and Some Aspects of Treatment*. ed. Hunt, B. L., Edinburgh (1966), p. 103.
- 4 ARMALY, M. F. (1965). *Arch. Ophthalm.* (Chicago) **73**, 11.
- 5 HOLLOWES, F. C. and GRAHAM, P. A., in *Glaucoma, Early Detection and Some Aspects of Treatment*. ed. Hunt, B. L., Edinburgh (1966), p. 24.
- 6 HARRINGTON, D. O. and FLOCKS, M. J. (1955). *Amer. Med. Ass.* **157**, 645.
- 7 GLOSTER, J. and BUCHANAN, W. M. (1965). *Brit. J. Ophthalm.* **49**, 57.
- 8 MILLER, S. (1961). *Trans. Ophthalm. Soc. UK* **81**, 577.
- 9 PATERSON, G. (1961). *Trans. Ophthalm. Soc. UK* **81**, 561.
- 10 FRANCOIS, J. and HEINTZ-DE-BREE, C. (1966). *Amer. J. Ophthalm.* **62**, 1067.
- 11 GRAHAM, P. A. (1966). *Proc. Roy. Soc. Med.* **59**, 1218.
- 12 SUTCLIFFE, S. (1960). *Brit. Orthoptic. J.* **17**, 1.



## **Office of Health Economics**

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