scan. This would ensure that recurrences of infection indicating the need for further imaging are detected.

Outpatient consultation and imaging services would need to be expanded considerably if all children with a proved urinary tract infection were referred for investigation, and only a minority will be found to have abnormalities. Attempts have been made to define criteria for selecting those children who should be investigated.[14,15] When general practitioners used the criteria of fever, recurrent infection, infection persisting after treatment, infection with unusual or resistant organisms, or infection with enuresis to determine referral for investigation, abnormalities were found in 38% (58% of those who underwent intravenous urography or radionuclide scanning).[14] Until more refined criteria are available, facilities for accurate diagnosis of infection must be provided and general practitioners encouraged to use them.

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The sight test fee: effect on ophthalmology referrals and rate of glaucoma detection

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Abstract

***Objective*—To assess changes, if any, in the numbers of referrals and outcome of glaucoma referrals to the hospital eye service since the introduction of the sight test fee on 1 April 1989.**

***Design*—Review of referral records and clinical notes.**

***Setting*—Referrals to the Bristol Eye Hospital.**

***Subjects*—51 919 patients referred to the Bristol Eye Hospital between 1984 and 1992. 9438 case notes of patients referred between 1987 and 1991 were examined in detail.**

***Main outcome measures*—Numbers of referrals; rate of adult true positive glaucoma referrals.**

***Results*—Referrals to the Bristol Eye Hospital were between 13·7% and 19·0% fewer than expected after the introduction of the sight test fee. True positive glaucoma referrals were reduced by the same proportion.**

***Conclusions*—The numbers of patients being identified as requiring treatment or follow up for potentially blinding glaucoma have declined by nearly one fifth since the introduction of the sight test fee. An increased prevalence of preventable blindness may result.**

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Introduction

The sight test is the only existing means of screening adults in Britain for sight threatening but treatable ocular diseases such as glaucoma. Over 80% of glaucoma referrals to ophthalmologists are initiated as a result of screening during routine sight tests.[1] Unconditionally free sight testing was withdrawn in the United Kingdom on 1 April 1989.

Concern was expressed that the introduction of a sight test fee would deter people, particularly elderly people, from having sight tests. It was suggested that as a consequence the rate of detection of blinding but potentially treatable ocular diseases such as glaucoma would fall.[2] The effect of the sight test fee on the rate of detection of eye disease has not been investigated. We therefore tested the hypothesis that there had been no change in the number of referrals to, or rate of identification of glaucoma at, the Bristol Eye Hospital since the introduction of the sight test fee.

Subjects and methods

Records of referrals to the Bristol Eye Hospital were examined for the number of referrals received each year during 1984 to 1992. Referral data from before 1984 were not available. The case records of adult referrals received between 1 July and 31 December each year during 1987 to 1991 were targeted for examination. A sample of these records was examined to determine the outcome of referrals for suspected glaucoma. Adult referrals were targeted because sight tests on children are still funded by the NHS.

There is a latency of up to six weeks between the identification of suspected disease by an optometrist and receipt at the hospital of a referral from the patient's general practitioner. To ensure that we were comparing referrals initiated after the sight test fee was introduced with those initiated before we targeted referrals received between 1 July and 31 December of each year during 1987 to 1991. The case records of patients referred with suspected glaucoma were examined to determine whether the referral was a true positive referral. Suspected glaucoma was defined as mention in the referral letter of glaucoma, abnormal intraocular pressure, optic disc changes compatible with glaucoma, family history of glaucoma, or field loss compatible with glaucoma. True positive cases were those in which the patient was noted at the first clinic visit to require follow up for confirmed or suspected

glaucoma, ocular hypertension, or low tension glaucoma.

True positive glaucoma referrals represent about 6% of all new ophthalmic referrals.[1] From this we calculated that a minimum sample size of 1500 referrals from each of the targeted six month periods was required to detect with 95% confidence a 10% reduction in the number of true positive glaucoma referrals being received in any of the targeted periods. A sampling protocol was devised to allow identification of up to 1800 referrals per six month period. Altogether 9438 of the 14657 referrals received in the five six month periods were examined. An estimate of the total number of adult true positive glaucoma referrals received in each six months was obtained by multiplying the number identified from the sample by the sampling fraction.

Simple linear regression with confidence intervals and the χ^2 test were used for analysis.

Results

The table gives the number of referrals received per year between 1984 and 1992 and the numbers of referrals with 95% confidence intervals predicted from linear regression of those received between 1984 and 1988. Numbers of referrals from 1989 onwards fell below the number received in 1988 and also below or very close to the lower 95% confidence intervals for the predictions. With the exception of the slight upturn in 1991 the numbers of referrals in each year were 18-19% fewer than predicted.

Actual and predicted referrals to Bristol Eye Hospital during 1984-92 and estimated true positive glaucoma referrals in each of five six month study periods

Year	Actual No of referrals	Predicted No of referrals (95% confidence interval)	Adult true positive glaucoma referrals (July to December each year)	
			Estimated No	% Of all referrals
1984	5042	—	—	—
1985	5020	—	—	—
1986	5420	—	—	—
1987	5934	—	169	5·5
1988	6466	—	181	5·7
1989	5487	6705 (6027 to 7383)	117	5·0
1990	5735	7081 (6214 to 7984)	157	5·3
1991	6439	7457 (6396 to 8519)	196	6·3
1992	6376	7834 (6574 to 9093)	—	—

The 6466 referrals in 1988 exceeded the number (6123) predicted from linear regression of trends between 1984 and 1987. This higher than expected total, however, was well within the 95% confidence interval of the prediction (5091 to 7145 referrals).

From the sampled notes the proportion of referrals which were adult true positive glaucoma cases averaged 5·6%. There was no significant variation in this proportion over the five years (table) (χ^2=5·47; df=4; P=0·34).

Discussion

Before 1 April 1989 routine sight tests performed by either optometrists or ophthalmic medical practitioners in the United Kingdom were funded by the NHS. Unconditional funding was withdrawn after that date. Subsequently around 60% of tests have been performed privately at an average cost of £13.20 each.[3] Free tests have remained available to people aged under 16 (or under 19 if in full time education), those receiving income support, patients with diabetes mellitus, glaucoma patients and their first degree relatives aged over 40, patients requiring complex lenses, and those registered either partially sighted or blind.

The sight test is the only existing means of screening adults in Britain for ocular disease. Glaucoma is a prevalent chronic and incurable disorder, occurring in 7% of people aged over 75.[4] Owing to predicted demographic changes the incidence of this condition is expected to increase. Glaucoma is an important cause of blindness, accounting for up to 15% of new blind registrations.[5-7] Unlike many other causes of blindness, glaucoma is treatable if identified in its early, usually asymptomatic stages.[8-10] Up to 90% of confirmed cases of glaucoma are first suspected as a result of screening during a routine sight test.[1 11 12] True positive screening referrals are therefore the source of the vast majority of cases of glaucoma.

Concern was expressed that introducing a fee would deter people, especially elderly people, from having sight tests.[2] It was hypothesised that fewer tests would result in less screening, that fewer patients would be referred to the hospital eye service, and that important sight threatening diseases such a glaucoma would remain untreated.

The effect of introducing the sight test fee on either the rate of referral of patients with suspected eye disease or the rate of identification of serious eye disease such as glaucoma had not been determined. We measured the total number of referrals and the number of adult true positive glaucoma referrals being received as a means of detecting any such shifts. Estimates of the effect on the number of sight tests being performed cannot be verified because no official records are kept of private tests.[3 13 14]

A total of 979 (15%) fewer referrals were received at the Bristol Eye Hospital in 1989 than in 1988. Some 1·8 million extra sight tests were performed in the 15 months leading up to the introduction of the fee.[14] Despite this, however, only 343 (5·6%) more referrals than predicted were received in 1988. The reduced totals from 1989 onwards should not therefore be attributed to early referral.

The proportion of all referrals which were adult true positive glaucoma cases did not vary significantly between 1987 and 1991 and averaged 5·6%. Between 13·7% and 19·0% fewer than expected referrals of all kinds were received after the introduction of the sight test fee. The rate of identification of glaucoma was therefore correspondingly reduced after the introduction of the fee. From these figures, in 1992 a total of 356 true positive glaucoma referrals would have been received at the Bristol Eye Hospital; 438 would have been predicted from trends observed before the introduction of the fee. This shortfall represents one case a year per 10000 of the population.[15] If this local reduction in the rate of glaucoma detection reflects a sustained nationwide phenomenon an increased incidence of preventable blindness can be anticipated.

Clinical implications

- The sight test is the only existing means of screening adults in Britain for treatable but potentially blinding ocular diseases such as glaucoma
- Since 1 April 1989, 60% of adults have had to pay for sight tests
- During 1989-92 up to 19% fewer than expected new patient referrals were received at the Bristol Eye Hospital
- True positive glaucoma referrals were also reduced by 19%
- The rate of identification of glaucoma has declined by nearly one fifth in Bristol since the introduction of the sight test fee
- An increased prevalence of preventable blindness may be expected

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Association of apolipoprotein E phenotypes with late onset Alzheimer's disease: population based study

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Abstract

***Objective*—To determine the association between the e4 allele of apolipoprotein E and Alzheimer's disease in a randomly selected population sample.**

***Design*—Cross sectional population based study.**

***Subjects*—980 people aged 69 to 78 (349 men, 631 women).**

***Setting*—Population of Kuopio, eastern Finland.**

***Main outcome measures*—Presence of e4 allele and diagnosis of Alzheimer's disease by detailed neurological and neurophysiological evaluation.**

***Results*—46 (4·7%) subjects were classified as having probable or possible Alzheimer's disease. The frequency of the apolipoprotein E e4 allele was 0·359 in patients with Alzheimer's disease and 0·165 in subjects without dementia ($P<0·0001$). The prevalence of Alzheimer's disease was 2·9% in subjects with no e4 alleles, 7·6% in subjects with one e4 allele, and 21·4% in subjects with two e4 alleles of apolipoprotein E.**

***Conclusions*—Allele e4 of apolipoprotein is associated with Alzheimer's disease in a dose-response fashion in a randomly selected elderly population.**

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Introduction

Alzheimer's disease is a leading cause of dementia in elderly people. Genetic factors have an important role before age 60, when the disease is caused either by a mutation in the amyloid precursor protein on chromosome 21 or, more commonly, by an unidentified gene on chromosome 14.[1-2] Evidence is accumulating that apolipoprotein E is important in late onset Alzheimer's disease. Three common alleles, e2, e3, and e4 determine the six apolipoprotein E phenotypes E2/2, E2/3, E2/4, E3/3, E4/3, and E4/4. Plasma apolipoprotein E phenotypes modulate lipoprotein concentrations, particularly that of low density lipoprotein cholesterol.[3,4] Furthermore, phenotypes E4/4 and E4/3 have been associated with the risk of myocardial infarction and coronary heart disease,[5-7] particularly in young people, although there is some controversy about this.[8]

The first evidence that e4 allele of apolipoprotein E could be associated with Alzheimer's disease was published by Pericak-Vance *et al.*[9] They showed a genetic linkage to chromosome 19 in affected members of families with a history of Alzheimer's disease after the age of 60. Recently, several studies based on clinical series have shown an association between the e4 allele and Alzheimer's disease in elderly subjects.[10-14] These studies indicate that 30-40% of all Alzheimer's disease cases could be attributed to the allele. Thus, it is the most common risk factor for Alzheimer's disease known so far.

All the studies that have investigated the relation between apolipoprotein E polymorphism and Alzheimer's disease have included highly selected patients and corresponding controls. Therefore we investigated whether the association of the e4 allele with Alzheimer's disease could be found also in a randomly selected elderly population living in eastern Finland. The Finnish population is of particular interest because the frequency of the e4 allele is high in this population.[15]

Subjects and methods

We selected subjects for this study from those participating in a population based study investigating risk factors and prevalence of atherosclerotic vascular disease in elderly people. The baseline study was conducted in Kuopio, east Finland in 1986-8, and it included 1300 subjects aged 65-74 years who were randomly selected from the inhabitants of Kuopio.[16] The follow up study was performed in 1990-1, on average 3·5 years after the baseline study. Of the 1192 subjects still alive, 980 participated in the follow up examination, which also included screening for dementia. All subjects gave informed consent and the study was approved by the ethics committee of Kuopio University Hospital.

Dementia was diagnosed in three phases (box). In the first phase we used five neurophysiological tests to identify people who were potentially demented (box). These tests have been validated and a detailed descrip-