

METHODS FOR THE EARLY DETECTION OF POTENTIALLY
BLINDING EYE CONDITIONS

Report on a Working Group convened
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1. INTRODUCTION

Early detection, it hardly needs saying, is all-important in acute disorders such as ophthalmia neonatorum and other forms of purulent conjunctivitis, acute glaucoma or acute iritis. What is not as clearly recognized, is that early detection is almost as essential in many other affections that do not run an acute course. As views differ on the value of early detection in certain affections, actual practice may well vary in different countries and from one clinic to another.

In the light of the above considerations the Regional Office for Europe of the World Health Organization, as an initial step in a programme of activities for the prevention of such conditions, convened a Working Group, which met at Copenhagen from 7 to 11 December 1970. The Group consisted of leading specialists concerned with this field. They had at their disposal detailed reports on various European countries, systematically covering current ophthalmic practice there. Professor A. Sorsby was elected Chairman of the Working Group and at the same time acted as Rapporteur. A list of the working documents is given in Annex I and a list of the participants in Annex II.

The working papers presented confirmed the considerable variations in practice from country to country. These differences extend not only to the range of conditions in which early diagnosis is sought, but to the actual detection procedures used. An outstanding case in point is the place of tonometry in screening procedures for glaucoma. Here, there are substantial differences of opinion as to its value, possibly because different countries have different objectives.

Both in the papers and the discussions it became clear that early detection is of great significance from the public health standpoint. Although, in some affections - typically most hereditary diseases, the embryopathies, and some toxic disorders - early detection may not do much to influence their course, it may well give valuable guidance on their prevention. In this context the term early detection has a different meaning from its normal implication of establishing pointing signs and symptoms in an individual patient: it comes to stand for the recognition of groups at risk in particular communities.

Three specific issues emerged in the course of the Group's discussions. In the first place, the administrative structure of the medical services, the facilities available as regards hospitals and personnel and the concentration of the population all help to determine the possibilities for early detection. Ophthalmological practice is thus only one factor in such differences as prevail between centres. Secondly, there are considerable national differences in the attitude to mass screening programmes. Thirdly, the cost-benefit analysis is everywhere a significant determining factor when it is a question of initiating exploratory investigations into the value of early diagnosis and the techniques to be employed. Consequently such investigations must clearly be subject to local requirements.

2. GENETICALLY DETERMINED CONDITIONS

2.1 Individual aspects in children

In only three genetically determined affections - excluding squint with its amblyopia - is early detection of clinical importance. Of these three, two, buphthalmos and retinoblastoma, are genetically determined only occasionally; the third, galactosaemia, appears to be uncommon. In addition, early decompression in the hereditary craniostenoses may perhaps prevent the onset of optic atrophy.

2.1.1 Buphthalmos

This is a well recognized affection, and the importance of early detection and treatment is well appreciated. At present diagnosis before the clinical picture is definite does not appear to be feasible.

2.1.2 Retinoblastoma

Broadly speaking, bilateral cases are now all regarded as genetically determined, the unilateral cases as sporadic. There are, however, important modifying circumstances. Transmission of bilateral cases in survivors is somewhat limited by the penetrance being incomplete, so that the chance of transmission is not 50 per cent but about 40 per cent. Furthermore the incomplete penetrance may still give a unilateral retinoblastoma. This "irregular dominance" may thus lead to pedigrees in which there is an affected child from apparently normal parents, one of whom does, however, have a positive family history of retinoblastoma. A unilateral retinoblastoma, while typically sporadic, may thus be merely the early stage of a bilateral dominant affection or, less commonly, an incompletely expressed dominant bilateral affection, or even an incompletely expressed new mutation.

It has been estimated that some 15 to 20 per cent of sporadic unilateral retinoblastomata are in fact new mutations, so that 40 per cent of 15 to 20 per cent (i. e., 6 to 8 per cent of these offspring of patients with unilateral retinoblastoma) could be at risk.

All cases of unilateral retinoblastoma thus call for frequent examination for any evidence of involvement of the second eye, for early detection holds out the prospect of adequate radiotherapy or other therapeutic measures. This is now, indeed, common clinical practice. In sporadic cases it is a necessary precautionary measure, but in genetically determined cases such supervision is essential if a lethal outcome or total blindness are to be avoided.

2.1.3 Galactosaemia

In this recessive disorder an enzyme defect prevents the conversion of galactose into glucose. (This enzyme defect is apparently widespread in nature, as shown by a galactose negative variety of *Bacillus coli*.) The high galactose concentration in blood and urine leads to severe toxic effects, including cataract, which generally develops in the fourth week of life. Early detection and adequate dietetic control may obviate severe damage - ocular, mental and physical.

Galactosaemia, like phenylketonuria, is one of the few controllable inborn metabolic disorders. Systematic analysis of the urine of neonates is practised in highly developed maternity units, but does not appear to be a routine in most institutions. The occurrence of lens changes in about 75 per cent of cases - easily recognized from the fairly characteristic early manifestations, simulating a drop of oil in the centre of the lens - may not often be of critical value in the diagnosis which is readily made on the findings in the urine. Early detection is none the less urgent, for early lens changes are likely to be reversible.

2.2 Individual aspects in adults

The outstanding relevant affection is glaucoma. Its substantial genetic aspects are dealt with in chapter 6.

2.3 Recognition of genetic disease in the foetus

2.3.1 Tay-Sachs' disease

Following on the finding that Tay-Sachs' disease is characterized by the absence of hexosaminidase A and that amniotic fluid taken by amniocentesis between the third and fourth month of pregnancy will reveal this abnormality, therapeutic abortion becomes possible where the possibility of a second affected child arises.

2.3.2 Down's syndrome ("Mongolism")

The characteristic chromosomal defect of Down's syndrome can likewise be established in the amniotic fluid by amniocentesis.

2.4 Public health aspects

2.4.1 Hereditary degenerative disorders (abiotrophies)

Ophthalmologists, even more than neurologists, are well acquainted with the hereditary degenerative diseases, if only because of the high frequency of retinitis pigmentosa. It is becoming increasingly likely that there is no real line of demarcation between congenital hereditary defects and the abiotrophic disorders. This has been emphasized in recent years by both laboratory studies such as those on the histology of the retina in

animals affected with retinal dystrophy, and clinical studies such as those on the essential similarity of retinal aplasia (Leber's congenital amaurosis) with retinitis pigmentosa. The possibility is emerging that some of the so-called senile degenerations of the fundus are also genetically determined. These considerations are not altogether theoretical and serve to emphasize the significant place hereditary affections now hold in ophthalmology. They also call for increasing endeavour to recognize the carrier state where possible.

2.4.2 The carrier state

Of late, the search for minimal manifestations of pathogenic genes, that is, the recognition of the carrier state, has extended to biochemical and serological as well as to morphological traits. This search has been helped by appreciation of the fact that genes are pleiotropic in effect: that is, they influence more than one trait, and these are not necessarily morphological. It is a matter of some interest that some of the tell-tale minor anomalies now recognized as evidence of the carrier state were known to earlier generations of clinicians and, because of their innocuousness, were regarded by them as "physiological variations".

The term "carrier state" - with its suggestion of association with the carrier of infectious disease - is not altogether satisfactory. Moreover, it has no precise meaning. Partial manifestations in heterozygotes in recessive autosomal disorders are more strictly aspects of intermediate rather than recessive inheritance. Likewise, partial manifestations in women carriers of recessive sex-linked affections are aspects of intermediate rather than recessive sex-linkage. The partial manifestations seen with dominant genes are aspects of expressivity and are often not considered in discussions on the carrier state. The carrier state is sometimes even advantageous: the sickle-cell trait carries with it greater resistance to infection by malignant tertian malaria. In strict logic the term could be applied to the possessor of any pathogenic gene, whether manifest or silent. Here the term used in its clinical context: the search for minimal, often non-pathological, anomalies (morphological, serological or biochemical) which indicate that the individual carries a pathogenic gene.

Evidence of the carrier state is readily available to the ophthalmologist alerted to its existence and significance. In the dominant disorders there is a whole range of incomplete expression in the colobomatous defects (extending from anophthalmos to a minimal iris coloboma), in aniridia, in macular cyst and possibly also in glaucoma. In recessive disorders, a histological anomaly (vacuolation of lymphocytes) is seen in the carriers of Tay-Sachs' disease and a biochemical anomaly (diminution of β -lipo-protein) in the carriers of the Bassen-Kornzweig syndrome. The evidence is particularly striking in sex-linked fundus affections: sex-linked retinitis pigmentosa gives a characteristic tapetal reflex in carrier women. The fundus appearances in the carriers of choroïderæmia and of sex-linked albinism are equally striking and pathogenic.

2.4.3 Genetic counselling

The recognition of the existence of genetic disease in individuals, and where possible of the carrier state, is of paramount importance and of course, the responsibility of the ophthalmologist. This is the basic requirement for adequate genetic counselling, which itself calls for expert knowledge of the rapidly expanding field of clinical genetics.

It would seem that adequate facilities are needed for two particular groups at risk: in the first place, for those with a family history of known or potential hereditary disorders (in this latter group, recognized or potential carriers are to be included); secondly, and less urgently, for partners in consanguineous marriages.

2.5 Recommendations

- (1) The attention of ophthalmologists should be drawn to the substantial frequency of genetically determined affections, and to the possibilities of recognizing incompletely expressed dominant disorders and the carrier state in some of the recessive affections.
- (2) There is an immediate need for genetic counselling units under expert clinical geneticists who should have full laboratory facilities at their disposal. Where such units are available ophthalmologists could well leave to them the responsibility for giving genetic advice.

3. EMBRYOPATHIES

3.1 General observations

Congenital syphilis is the classical example of an embryopathy, well recognized long before the designation "embryopathy" was evolved in recent decades. There is less adequate recognition of other pathogenic influences emanating from the mother. The concept of a placental barrier as a protective mechanism for the embryo and "intra-uterine inflammation" stressed two contrary processes. It is clear, now, that infecting organisms other than the spirochaete can pass through the placenta into the embryo and that other processes besides infection can damage the developing embryo: iatrogenic agents (such as thalidomide, quinine and possibly many others); systemic disturbances (such as diabetes and toxæmia); constitutional incompatibilities (such as Rh factors); physical agents (such as radiation); and various unrecognized disorders (such as most of those that lead to habitual miscarriage). The pathology of the embryo is still largely an unexplored discipline.

It is clear that the embryo is subject to as wide a range of disease processes as the adult, extending from mild disturbances at one extreme to death at the other. Miscarriage early in pregnancy and still-birth later on thus represent lethal disorders, while non-lethal disorders may, theoretically, range from a minimal anomaly to multiple defects. Whether every potential pathogen may have both mild and severe effects or whether some pathogens are always limited in their effect is as yet not known.

At present, embryopathy implies a generalized disorder which may or may not include ocular manifestations. It is likely that some purely ocular malformations will ultimately be seen as the result of limited embryopathies; this is suggested by such observations as the production of limited ocular malformations in experimental vitamin A deficiency in the pig. It is also clear that the age of the embryo at which it is subject to the pathogen is all-important: early on in pregnancy the whole embryo will be susceptible, later, only specific organs at critical stages in their development will suffer from a noxious agent of a transient character.

Clinically, the embryopathies - whether extensive or limited - are at present seen only in their end-stage in live births. It is conceivable that some pathogenic processes may have delayed effects: this is well established in congenital syphilis and may perhaps apply to toxoplasmosis. For the present, the question of early detection thus hardly arises in the case of embryopathies. Even the public health aspect of early detection is as yet of limited significance, for there is nothing to suggest that infective agents other than the spirochaete persist to produce damage at more than one pregnancy. Constitutional incompatibilities, such as those of Rh factors, will of course persist, but these are not known to produce ocular malformations and are, in any case, essentially a genetic problem. In practical terms, early detection in the embryopathies is thus largely limited to the recognition of mothers at risk and babies at risk.

3.2 Mothers at risk

3.2.1 Transmitted maternal infections

Syphilis

Current practice everywhere recognizes the imperative need for intensive specific treatment. The welfare of the mother and of the baby calls for this no less than the public health requires the elimination in the mother of a potentially persistent infection that may affect later pregnancies.

Rubella

Any woman of child-bearing age is at risk unless protected by having had rubella early in life. It is not known whether the immunity so obtained persists throughout life, but the rubella vaccine now available is probably an effective protection for the critical years if given to girls aged 11-13

years who have not earlier contracted rubella in the natural way. Such vaccines are never given to women in the early months of pregnancy, for they would probably be as dangerous as a natural attack of rubella.

The administration of gamma-globulin to non-immune pregnant women exposed to the risk of rubella is of doubtful value.

Toxoplasmosis

The high incidence of positive cutaneous reactions in the general population necessitates serological tests. As these latter are a measure of the circulating anti-bodies, it is possible that the most definitely positive reactions would indicate that the level of maternal anti-bodies is sufficiently high to protect the foetus from infection. A further consideration is that pyrimethamine used in treatment might be teratogenic. It is also possible that only acute toxoplasmosis during pregnancy is relevant.

There would appear to be no standard procedure for the detection and management of toxoplasmosis-positive results observed during pregnancy. It is ignored in some countries, in others it seems to be searched for and treated as a routine, and in yet others only occasionally.

Virus diseases other than rubella

The evidence of virus diseases other than rubella as a cause of malformations is still indefinite. An affection that also calls for consideration is cytomegalic inclusion disease. As this is a cause of still-birth (as also of death in infants during the first weeks of life), maternal transmission seems to be a likely route of infection.

3.2.2 Systemic disease

Diabetes

This has serious implications for the survival and health of the baby. It is not clear that ocular malformations occur.

Toxaemia of pregnancy

Much the same applies.

Teratogenic disorders

Among the older drugs quinine intoxication and among the newer ones thalidomide medication come into question only retrospectively after the birth of an affected child. There is nothing to suggest that the toxicity persists in subsequent pregnancies, though there is the theoretical possibility that persistent or repeated medication might carry teratogenic risks.

3.3 Affected babies

The possibility of early diagnosis only arises in congenital syphilis, and this is not always obvious.

In babies affected by the other disorders discussed, the malformations are generally obvious at birth. While toxoplasmosis can give rise to severe lesions, it is the rubella syndrome which is particularly distressing.

As regards the rubella syndrome, it is clear that at present the elimination of a substantial quota of severe ocular and systemic malformations could be achieved by therapeutic abortion in cases where rubella is contracted early in pregnancy.

3.4 Babies at risk

3.4.1 Premature babies

The relationship of retrolental fibroplasia to marked prematurity and the significance of excessive oxygen therapy in precipitating the affection is well known. It appears that spasms of the retinal arteries are an early sign. This makes systematic ophthalmoscopic supervision essential in all markedly premature babies and particularly important in incipient or developing retrolental fibroplasia.

The significance of prematurity and immaturity in congenital optic atrophy, and possibly other congenital defects, still needs to be assessed.

3.4.2 Babies with perinatal disorders

Anoxia and the complications of prolonged labour are the outstanding examples of this group of as yet ill-defined "birth injuries". The effects are likely to be generalized rather than purely ocular and may be particularly distressing.

Where infections are concerned, the early signs of purulent conjunctivitis (ophthalmia neonatorum) are obvious and are now readily brought under control.

3.5 Administrative aspects

It appears that in some highly developed maternity units expert ophthalmological examination of all neonates is a routine measure. Nowhere is there statutory ophthalmological examination of all new-born babies, though in actual practice this is occasionally achieved. At most units there is a variable degree of expert supervision of babies at risk, but the available services vary very considerably.

3.6 Clinical considerations

The administrative gaps in the provision of services taken together with our inadequate knowledge of the etiology of the embryopathies (using the term in its broadest sense) make practical measures for early diagnosis difficult. It would seem that much clinical and laboratory work is needed before such measures can be developed. A beginning would appear possible on the lines of the following recommendations.

3.7 Recommendations

- (1) A pilot survey should be made in several special care units. Expert ophthalmological examination and follow-up should be undertaken as a routine to establish the significance of prematurity, immaturity and distress at birth as a cause of congenital anomalies.
- (2) Studies are also needed of apparently normal mothers who have given birth to babies with ocular malformations.
- (3) Ophthalmological advice should be made readily available at maternity and child welfare centres.

4. SQUINT AND AMBLYOPIA

Squint, a cosmetic problem throughout history, presents, as such, no substantial surgical difficulties today. There are still outstanding issues on the management of the relatively uncommon vertical deviations, but the overriding consideration is the prevention and treatment of amblyopia. Amblyopia associated with squint is an important cause of monocular loss of vision. Previously regarded as a complication of squint (as the result of the child's suppression of diplopia consequent on the squint) it is now seen as an independent anomaly: a failure in the development of adequate binocular vision. It is to this failure that the sequel of suppression, amblyopia and squint must be ascribed. In this currently held view, there is a sharp distinction between squint seen early in infancy, and that first seen at four years of age or later. This latter form of squint is typically accommodative in origin, is devoid of amblyopia and readily responds to the classical methods of treatment. It is the squint of infants which is the problem today.

4.1 Difficulties in diagnosis

At present, assessment of binocular vision and of amblyopia is entirely subjective. The only objective sign is the onset of squint. Early detection - so greatly dependent on the subjective features - is

thus limited by the age and mental development of the infant. It is therefore all the more important to recognize the earliest signs of an actual squint in infants. In particular, attention needs to be paid to intermittent squint when reported by parents. Simple tests such as the cover test and the position of corneal reflexes should help and are within the competence of paramedical personnel. However, none of these tests are, of course, a measure of amblyopia.

4.2 The incidence of squint and of amblyopia

Reports on the incidence of squint in infancy and childhood are rather conflicting. They vary between 3 per 1000 to 6 or 7 per 100. It is possible that there are differences as between countries, but undoubtedly much of the discrepancy is due to lack of uniformity in the criteria used. Adequate data on the incidence of squint, and of amblyopia in critically observed series are needed, as indeed are systematic studies on the epidemiology of the affection.

4.3 Treatment of amblyopia

The simplest procedure is occlusion. This calls for no specialized techniques such as those required in orthoptic treatment or in pleoplics. These specialized facilities are not always readily available. They appear to have been developed more intensively in Central and Eastern Europe than in the Western and in the Scandanavian countries. At some centres in Czechoslovakia, Italy, Poland and USSR there are residential schools with hospital facilities. Detailed and critical assessment of the results obtained is needed.

The crucial issue in most countries is in getting infants with amblyopia and latent or indefinite squint to treatment centres. The medical services for children under school age are nowhere as adequate as the school medical services are, so that apart from diagnostic difficulties, there are variable but considerable shortcomings in contact between parents and the treatment centres. Where nursery schools are available on an extensive scale some of the difficulties in communication can be readily overcome. Elsewhere, there is inevitably much reliance on infant welfare centres, but these are not always able to provide the necessary ophthalmic guidance.

To overcome the lack of contact between parents and ophthalmic treatment centres, propoganda has been used among parents in Sweden and in the Federal Republic of Germany. Even mass screening has been attempted. It would seem that more effective results can be obtained by ensuring that the necessary technical knowledge for early detection is available to general practitioners and paramedical personnel who come into professional contact with infants and children.

4.4 Recommendations

(1) It is desirable that all infant welfare centres, whether well-baby centres or follow-up centres for babies at risk, should be able to tell the groups that are at risk from squint and amblyopia. While full epidemiological studies are still to come, the risk of squint is definite in the following categories:

- (a) infants with a family history of squint. It is likely that squint is determined by polygenic inheritance. A history of squint in a sib, in either of the parents or in their first and second degree relatives is therefore significant;
- (b) infants with multiple congenital defects;
- (c) infants with spastic palsy;
- (d) infants with debilitating disorders.

(2) Co-operation of general practitioners needs to be pursued actively. General practitioners should know of the groups at risk and of the danger of delay in treatment.

5. REFRACTION ANOMALIES

In all countries, the school medical service can be relied upon to carry out the necessary screening of children at school age. Under school age, the significant error of refraction to be considered is severe myopia. This is a possibility in infants with a history of marked prematurity and may also occur in infants with the same sort of family history as for squint.

6. GLAUCOMA

6.1 Diagnostic procedures in early glaucoma

6.1.1 Tonometry in mass screening

During the past twenty years large numbers of people, mostly over the age of 40, have been screened for glaucoma by tonometry. The

conflicting results reported from different centres, arise in part from the lack of any agreement as to what constitutes normal tension and, in part, from the different ways in which the glaucoma suspects are followed up. Normal tension is known to show diurnal variations and these possibly also vary with age. The difficulty of interpreting tonometric readings obtained in screening investigations is shown by the fact that in some countries night hospitals have been found necessary to assess diurnal variations and, in others, even more prolonged stay for further observations. While the significance of markedly raised tension as evidence of glaucoma is of course beyond question, there appears to be growing scepticism as to the value of borderline readings. The incidence of false positives may be as high as 90 per cent when such patients are investigated more fully or kept under prolonged observation. With lack of adequate criteria as to what constitutes normal tension, the high incidence of false positives, and a substantial incidence of false negatives (in that some patients passed as normal have developed glaucoma), it is clear that tonometry as a diagnostic tool for the detection of early glaucoma is not sufficiently promising to justify its use for mass screening. On the accumulated evidence now available, the value of tonometry is not very different from that of the provocative tests used clinically in individual patients suspected of glaucoma.

6.1.2 Screening of the central field by static stimuli in individual patients

It seems likely that the classical Seidel and Bjerrum signs of chronic glaucoma can be resolved into less damaging but equally characteristic field defects. The development of the newer type of central field screener - such as Friedmann's Visual Field Analyser - has made exploration of the field a relatively simple clinical procedure. Such screening is far more specific and sensitive than tonometry and the incidence of false positives is probably not more than 10 per cent.

It would therefore seem that a first step in the investigation of suspected glaucoma could well be assessment of the central field, much as taking visual acuity is in the routine examination of the eye. Screening of the central field might, in fact, be part of such routine examination, particularly in patients over the age of 40. Critical studies on the scope and limitations of the available central field screeners are still needed.

6.2 Groups at risk

6.2.1 Age factor

Reasonably enough, mass screening by tonometry has concentrated on age-groups over 40. But glaucoma at younger ages is not a clinical curiosity, as is shown by the designation of juvenile glaucoma. Such glaucoma often runs a rapid and severe course. This, in itself, would justify central field screening as a routine procedure at all ages.

6.2.2 Genetic considerations

As distinct from many older pedigrees showing dominant transmission of glaucoma, recent studies on the families of unselected glaucoma patients has revealed a high incidence of the affection in immediate relatives. This is generally recorded as about 20 per cent, while one substantial report on 104 consecutive cases gave an incidence of 46 per cent. Clear simple dominance is not always present and there is evidence of simple recessive inheritance in some cases. It is, however, likely that the commonest type of inheritance is polygenic rather than monofactorial. Mass tonometric screening has given similar results, showing the high frequency of glaucoma in relatives of glaucoma patients, so much so, that in many surveys, relatives are recognized as the one substantial group at risk.

Genetic studies have shown that open-angle and closed-angle glaucoma are separate entities, though occasionally the gonioscopic appearance of an open angle may be disturbed to simulate a narrow angle in an individual patient. Within the same family there is generally close similarity for age of onset and clinical course - a matter of considerable significance in early diagnosis.

Closed-angle glaucoma would appear to present no genetic problems different from those for the more common open-angle variety. The rare pigmentary glaucoma (sugar) is, however, different: it shows sex-linked inheritance. Whether there is a genetic factor in glaucoma capsulolenticularis is not known.

6.3 Glaucoma clinics

In most countries special glaucoma clinics are available at some centres. These clinics appear to have a rather wide scope of action. Some are research units, others are diagnostic centres and yet others are follow-up services. It would seem logical that at large ophthalmic centres the clinical units (the diagnostic and follow-up services) should indeed have sole responsibility for the glaucoma patients, much in the same way as diabetic units at general hospitals have the responsibility for all diabetics. Glaucoma clinics of this type are necessary because both early diagnosis of glaucoma and the follow-up of glaucoma patients can be very time-consuming, calling for more attention than can generally be given in most out-patient departments.

6.4 Recommendations

- (1) The value of using central field screeners in populations at risk of glaucoma calls for further assessment.
- (2) The function of the glaucoma clinic calls for further consideration.

7. OPTIC ATROPHY

7.1 Potential value of central field screening

By definition, optic atrophy is largely incurable. It is the end-stage of a series of etiologically diverse affections, most of which are not at present under control. Early detection, though of limited significance for the group as a whole, is therefore all the more important in the substantial proportion of cases where treatment may be effective: the toxic neuropathies and the optic nerve lesions arising from increased intracranial pressure.

In the toxic neuropathies central scotomata are frequently seen before the onset of optic atrophy. This group also includes tobacco-alcohol amblyopia. Central field screening has therefore some advantage over the classical methods of exposing scotomata.

In increased intracranial tension, the ophthalmoscope will of course disclose early papilloedema. This, however, may be lacking with pituitary tumours, in which optic atrophy may arise from direct compression. Central field defects may therefore develop before peripheral sector defects and screening of the central field may prove of considerable value. Controlled studies in radiologically diagnosed enlargement of the pituitary fossa are needed, as also in cases of suspected tumour compressing the optic tracts.

8. DIABETIC RETINOPATHY

8.1 Incidence

It is widely held that diabetic retinopathy is more frequent than it was in the recent past. Judging by the fairly full data for England and Wales, there has indeed been an increase in numbers, but this is likely to be the result of an increase in the number of diabetics who have survived as compared with earlier years and the steady increase in the elderly population. This is suggested by the fact that the rates per 100 000 for age-groups over 50 remained fairly stationary between 1955 and 1968. Adequate data on the lower age-groups are lacking.

The available rates per 100 000 show a marked excess in the incidence of diabetic retinopathy in women - an excess of the order of two to three times. This agrees with the greater incidence of diabetes in women after middle-life. Any sex-difference under 50 would appear to weigh on the side of men, but in them at any rate marked incidence of diabetic

retinopathy after 50, so striking in women, is lacking. With 22.5 per cent and 24.4 per cent of all cases, diabetic retinopathy holds the leading position amongst the causes of loss of vision in women at 50-59 years and 60-64 years. There is some evidence that retinopathy is more common in cases of diabetes that are not well-controlled, but this may mean nothing more than that these patients are more prone to retinopathy.

8.2 Early diagnosis

The characteristic miliary aneurisms (the punctate retinal haemorrhages recorded by older observers) appear to be common in diabetics of any standing. As they are generally extra-macular, silent and, furthermore, transient, they can hardly be regarded as early signs of retinopathy of serious import. This only arises when central vision is affected and vascular proliferative processes develop. As these in turn may remain stationary and perhaps also regress, it is clear that fairly indefinite and fluctuating degrees of severity are an essential aspect of the disorder and that early diagnosis is no sure guide to prognosis.

8.3 Treatment

It is difficult to assess the value of hypophysectomy and of light coagulation as methods of treating diabetic retinopathy. The bizarre course of the affection and the lack of adequate control material make judgement uncertain.

8.4 Genetic considerations

Diabetes itself is regarded as genetically determined. Whether the retinopathy is incidental or also genetically determined is not known. Family studies on the incidence of retinopathy in diabetics in both men and women (the latter being especially at risk) would be useful, if only that it offers the possibility of establishing criteria for the early diagnosis of progressive retinopathy.

8.5 Recommendation

Epidemiological investigations on diabetic retinopathy are needed, including a pilot survey on its possible familial incidence.

9. TOXIC DISORDERS

9.1 Pharmacological agents

9.1.1 Synthetic agents

Whereas quinine amblyopia has a considerable history, the synthetic preparations heralded by salvarsan, optochin and dinitrophenol have now created a substantial hazard. The first two of these agents carry a considerable danger of optic atrophy, while dinitrophenol gives cataract. The vast and increasing expansion of the pharmaceutical industry has made the danger of toxic effects from the use of new drugs an immediate and considerable problem necessitating varying degrees of control in different countries. In ophthalmology, optic atrophy and retinopathy are the outstanding complications, though lesser disturbances as in the cornea are probably not very uncommon.

9.1.2 Some toxic agents in use

It is known that a number of synthetic drugs have not been released on the market as they are likely to cause serious visual defects. There are, however, medications in fairly wide use which carry potential dangers. These are:

(1) Chloroquine and allied preparations. The retinotoxic effect of chloroquine was recognized in 1959. Retinopathy appears to develop only after prolonged dosage and there is evidence that the retinal pigment epithelium concentrates chloroquine. Once initiated, the retinal damage is probably irreversible and possibly progressive. Ophthalmological supervision is therefore essential. Ophthalmoscopically, the established lesion is pathognomonic in appearance. Early diagnosis is probably feasible by screening of the central field. Electroretinography does not appear to be of use.

(2) Thioridazine (Melleril). This phenothiazine is used widely. It is retinotoxic in high and prolonged doses, though considerably less so than the allied Piperdichlorophenothiazine ("N. P. 207").

(3) Ethambutol. This is one of the newer agents used in tuberculosis. It is known to produce central scotomata and disturbances in colour vision.

9.1.3 Agents with occasional ocular toxicity

A very large number of newer agents have been reported as giving ocular complications. The evidence is not always convincing and the frequency of established complications - for example with the sulfonamides - is apparently low. Further data are needed on the complications of local and general steroid therapy.

9.2 Other agents

Little is known of the ocular toxicity of agents other than medications and addictive drugs, such as tobacco, ethanol and methanol. Early detection is feasible in tobacco amblyopia and possibly also in the chronic forms of alcohol poisoning.

The dangers of oxygen therapy in retrolental fibroplasia are well recognized.

9.3 Recommendations

- (1) New drugs. In most countries some control of new pharmaceutical agents is now available. Central agencies to which the complications of new drugs are reported are also being developed. It is highly desirable that hospital units trying out new drugs should include ophthalmic supervision as a routine in their investigations.
- (2) Drugs known to have ocular toxic effects. Physicians using chloroquine, thioridazine, ethambutol or other agents (such as flouride) should ensure systematic ophthalmological supervision.
- (3) Scope of ophthalmic examination. Apart from routine examination, central field screening is necessary to disclose scotomata which are likely to be the earliest signs of lesions of the optic nerve or of the retina.

10. OTHER ASPECTS

10.1 General observations

In the surveys and discussions on four different fields, it appeared that little new could be adduced regarding early detection. The fields in question were traumata, neoplasms, infections, and the affections of old age.

10.2 Trauma

The early signs of trauma are unlikely to be overlooked in contusion or in perforating injuries. Radiation injuries, whether of the classical type such as glass-blower cataract or the newer forms such as radiation cataract in uranium mines call for preventive measures that are well known in the industries concerned. They pose problems of administration rather than individual supervision.

In no country does there appear to exist a fully developed industrial health service, but in most there is medical supervision at factories and workshops, the fullest coverage probably being in eastern Europe. In most western countries the ophthalmological services tend to concentrate on standards of visual acuity as safety precautions in particular industries. There is clearly need for the public health services to provide rather more systematic ophthalmological coverage in relation to industry.

10.3 Neoplasms

The three outstanding ocular neoplasms are retinoblastoma, choroidal melanoma and the epibulbar tumours. The first is fully discussed in 2.1.2. The second and third present clinical difficulties resolved by repeated examinations. Judging by recent reports, it is possible that choroidal melanomata are occasionally determined genetically, inheritance occurring in a simple dominant manner. Further observations are needed.

10.4 Infections

The urgent need for recognizing early signs of infections are well known. The advent of antibiotics has only emphasized this need. The danger today lies in the fact that the newer generations of ophthalmologists, who have not known the times when medicine was dominated by problems of infection, may overlook early signs because of their limited acquaintance with them. This is an educational problem that needs stressing.

10.5 Affections of old age

Most cataract and most macular lesions are seen in the elderly and, classically, they have been designated as "senile" disorders. As they affect only a very small proportion of the elderly, they are clearly not disorders of senescence, but merely disorders incidental to old age. Early signs are frequent enough, the course being very variable with both cataract and macular lesions. However, early diagnosis carries no advantage in the absence of adequate therapeutic measures.

11. CONCLUDING REMARKS

11.1 General observations

Though the outstanding considerations in the discussions were of necessity clinical and epidemiological, there were also, inevitably, aspects bearing on administration, the co-operation of patients, inter-professional contacts, professional training, dissemination of information and priorities in current and likely developments. Some of these call for further discussion.

11.1.1 Administration

This is largely a problem affecting the pre-school child, for in all countries there are considerable gaps in the clinical services available to infants under school age. This has already been stressed, and it is clearly not an exclusively ophthalmic problem. In ophthalmology it is a definite need in relation to such disparate conditions as genetic anomalies, embryopathies, perinatal disorders, squint in infancy and refractive errors. As the available ophthalmic services for pre-school children and existing clinical facilities for infants are limited, co-operation between them wherever possible needs to be encouraged and developed.

11.1.2 Co-operation of patients

This is primarily a question of facilities. Where adequate facilities exist it is likely that they will be used by the population. There are special problems in relation to children and much can be achieved by enlisting the interest of general practitioners and the staffs of infant welfare centres in specific ocular anomalies.

11.1.3 Inter-professional contacts

The general medical aspects of ocular diseases call for the more ready exchange of information between ophthalmologists and physicians than now generally occurs. The highly developed ophthalmic periodical literature has brought with it the disadvantage that relatively little of broad ophthalmic interest appears in the general medical journals. Isolation is a danger to ophthalmic training, practice and progress. More could perhaps be done to encourage the representation of administrative and scientific personnel in the highly specialized ophthalmic groups - such as those on squint - that are now being developed. Such contacts are clearly needed in the less specialized fields of general ophthalmology.

11.1.4 Centralization of information

More can be done in the way of centralizing information on genetic disorders, neoplasms and visual handicaps, as well as on industrial injuries and iatrogenic disease. Such information, of inestimable value for national purposes, will need some co-ordination in respect of standards and nomenclature if it is to be of equal international validity. While serving as guides for immediate action such data would also help in the rational assessment of research priorities. Any central agency of this type would need adequate contacts with epidemiologists as well as ophthalmologists.

11.1.5 Comparative statistical data on the incidence and causes of loss of vision in Europe

Statistics on blindness in different countries, supplemented by data from representative blind schools, would be valuable for any general reviews. Such returns are in the nature of mortality statistics and need epidemiological studies, of which few are available, to give adequate guidelines for further study.

11.2 General recommendations

11.2.1 Mass screening

Mass screening would appear to be of uncertain value judging by experience of tonometry in mass screening for glaucoma. The screening of populations at risk is more feasible and potentially rewarding.

11.2.2 Screening of populations at risk

In certain fields, such as glaucoma, the genetically determined disorders, infants requiring special care, squint and in iatrogenic and toxic hazards, the early screening of groups at risk should be carried out. In the pre-school population screening has to be fairly extensive pending the development of comprehensive medical services for all children under school age.

11.2.3 Genetically determined disorders

As already stressed, the significance of these disorders in present day ophthalmology is such that measures need to be taken to impress it on ophthalmologists. Moreover, adequately staffed genetic counselling centres should be readily available.

11.2.4 Determination of retinal and optic nerve functions

The advent of central visual field screeners is a significant clinical advance. It has made possible the rapid demonstration of scotomata indicative of anomalies of the retinal and optic nerve functions. The use of such screeners should become as essential a part of eye examination routine, as the taking of visual acuity is now, since the demonstration of early field defects may play a significant part in the diagnosis of early glaucoma and incipient optic atrophy.

The early detection of potentially blinding affections is of value mainly in potentially curable disorders. It would seem that the effort involved in searching for early signs and the patients who show them, far from being an academic exercise, is likely to contribute substantially to reducing the incidences of blindness. Clearly, new measures are needed in an age in which the infectious diseases causing blindness have been largely eliminated from the majority of countries in the European Region. New measures and additional knowledge are also needed for old disorders that are now of greater relative significance and for the new anomalies which are the by-products of public health, paediatric and pharmacological advances of recent years.

11.2.5 Need for a general public health approach

In preparing for the Working Group and in the Group's discussions, it became clear that the quest for early signs in present day ophthalmology, in both its individual and public health aspects, frequently calls for broader vistas than those that were adequate in classical clinical ophthalmology.

From all the above considerations it clearly appears that unnecessary loss of vision with its socio-economic implications is becoming an increasingly important problem in the European Region and that this should be brought to the attention of public health authorities at all levels.

New knowledge in this field can be best acquired through an interdisciplinary approach. There is no need to stress how much public health administrators can contribute to successful results from the co-ordinated activities of several disciplines.

New public health measures stemming from new knowledge in this field (screening for the prevention and treatment of various conditions leading to loss of vision), should also be given priority by public health administrators when planning services for the benefit of those concerned. At the same time rational use should be made of national manpower resources to this end.

ANNEX I

LIST OF WORKING DOCUMENTS

- EURO 0328/3 Report on a visit to the United Kingdom -
Dr P.A. Graham
- EURO 0328/4 Report on a visit to the USSR and Hungary -
Professor O. Litricin
- EURO 0328/5 Report on a visit to France and Belgium -
Dr A. Arruga
- EURO 0328/6 Report on a visit to Poland and Czechoslovakia -
Professor O. Litricin
- EURO 0328/7 Report on a visit to Sweden, Norway, Denmark -
Dr F. Adelstein
- EURO 0328/8 Report on visits to the Federal Republic of Germany,
Berlin and Austria - Dr S. Delthil
- EURO 0328/9 Report on a visit to Finland - Dr B. Nizetic
- EURO 0328/10 Report on a visit to Italy - Dr P.A. Graham
- EURO 0328/11 The genetic aspects of preventing blindness -
Professor D. Klein
- EURO 0328/12 Methods of early detection - Professor A.P. Nesterov

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