Dense Kayser-Fleischer ring in asymptomatic Wilson’s disease (hepatolenticular degeneration)

The Kayser-Fleischer ring is the single most important diagnostic sign in Wilson’s disease; it is found in 95% of patients. Virtually all patients with Kayser-Fleischer rings have neurological manifestations.1 Pseudo rings have been described in other conditions.1 The density of a Kayser-Fleischer ring correlates with the severity of Wilson’s disease.2 We describe a rare case of a dense Kayser-Fleischer ring in an asymptomatic patient with an extremely high liver copper content. The recent significant genetic advances, and the clinical implications are discussed.

Case report

At the age of 14 this 23 year old woman had an eversion of her left eye for painful ruboeic glaucoma following chronic retinal detachment, resulting from ANA positive iridocyclitis. Her optician referred her because over the past few years, her left prothetic eye had repeatedly needed an increasingly dense brown ring painted onto it, to match her remaining eye. On examination the visual acuity in the right eye was 6/6 with a heavily pigmented red brown Kayser-Fleischer ring (Fig 1). Her systemic and neurological examination were normal.

Baseline biochemistry, liver function, haematology, and cerebral magnetic resonance image (MRI) were normal. She was ANA positive 1 in 20, serum copper 11.6 μmol/l (normal 11–22), and ceruloplasmin 0.15 g/l (normal 0.9–2.6). Twenty four hour urinary copper 9.2 μmol/24 h (normal 0.9 μmol/24 h). Haematoxylin and eosin stained liver biopsy showed normal architecture. Orein and rhodanine stains showed patchy excessive copper binding protein, and copper within the hepatocytes. The quantified copper content of the sample was hugely elevated at 3000 μg/g.

The patient was referred to Birmingham and Midlands Eye Hospital, and treatment was continued with trientine dihydrochloride.2 The Kayser-Fleischer ring initially became denser but has faded considerably over the past 5 years; a thin rim still persists (Fig 2).

Reference


Rapidly developing intimal fibrosis mimicking giant cell arteritis

Temporal headache associated with a tender superficial temporal artery and decreased pulse on palpation are characteristics of giant cell arteritis. We report the clinical and biopsy findings in a patient in whom these symptoms were caused by a rapid developing intimal fibrosis.

Case report

A 51 year old woman presented with a 2 month history of a tender and painful left superficial temporal artery (STA). First she noticed a “thickened cord” on the left temple which felt pulsatile on palpation. Within 6 weeks the throbbing pulse disappeared and was followed by tenderness and pain. She also reported arthritic pain in the limbs and a morning cough over a 2 year period. She had smoked 40 cigarettes per day for 30 years. On examination the left STA felt hardened, knotted, non-pulsatile, and was slightly tender over a 2 cm distance (Fig 1, cross). There were no bruits on auscultation of major arteries. The facial and maxillary arteries were soft and such as super oxide dismutase.6 This could be a plausible explanation as to why such an extraordinarily high level of copper was bound safely in this patient’s liver.

Untreated Wilson’s disease has progressive, irreversible consequences, and ultimately causes death.7 The identification of a Kayser-Fleischer ring remains the most important clinical sign for the diagnosis of Wilson’s disease.

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follow up period and subsequent ESR and photomicrograph showing a Figure 2

be observed. Of elastic fibres. No thrombotic material could of collagen and concentrically arranged layers had led to tightening of the lumen consisted fibrosis (Fig 2). The thickened intima, which was considerably thickened, which minimised the chance of a false negative result. It was considered necessary to exclude an inflammatory cause, given the similarity of the presentation to giant cell arteritis. The biopsy was taken at the site where the STA was pulseless and most prominent (Fig 1). The tissue was examined using the serial block, serial section technique in order to minimise the chance of a false negative result. The histological appearances were those of a severely fibroblasted artery devoid of any inflammatory changes and consistent with arteriosclerosis. The intima was considerably thickened, the internal elastic lamina was preserved, and the media had some degree of fibrosis (Fig 2). The thickened intima, which had led to tightening of the lumen consisted of collagen and concentrically arranged layers of elastic fibres. No thrombotic material could be observed. The patient remained stable over a 3 year follow up period and subsequent ESR and CRP were normal. She continued having diffuse body pain.

Comment

GCA is a neurological emergency which, when left unrecognised and untreated frequently leads to permanent blindness. ESR can be normal in 5–30% of patients, but this is an exceptionally rare diagnosis in middle aged patients.

In summary, our patient presented with a clinical picture suggestive of vasculitic occlusion of the superficial temporal artery, polymyalgia, and cough. We present this case as an illustration that this clinical picture can result from rapidly developing superficial temporal arteritis without any evidence of inflammation.

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References


Fixed dilated pupil following deep lamellar keratoplasty (Urrets-Zavalia syndrome)

A fixed dilated pupil following penetrating keratoplasty is a well recognised if rare postoperative complication. We report a case of Urrets-Zavalia syndrome following a deep lamellar keratoplasty (DLK). To our knowledge this association has not been previously described.

The mydriasis following penetrating keratoplasty was first described by Castroviejo (Castroviejo R, personal communication) but it was Urrets-Zavalia who first published his observations on a series of six cases and suggested an association of fixed dilated pupil, iris atrophy, and secondary glaucoma.

The incidence of this syndrome is estimated at 5.8%, from pooled data on 445 eyes undergoing penetrating keratoplasty for keratoconus, of which 24 eyes developed a fixed dilated pupil. Davies and Ruben also found a similar incidence. However, other more recent studies find no cases, and some even question its continued existence. This may in part reflect improved surgical technique and differing diagnostic criteria.

The pupil can become abnormally dilated following penetrating keratoplasty for keratoconus, particularly if dilating drops are used. There are three main groups of pupillary dilatation:

(1) A pupil with normal light and near reaction which is at least 1.5 mm larger than its fellow unoperated eye. It fully constricts with topical miotics. An incidence of approximately 90% has been reported for this type of abnormality.

(2) An unreactive paretic pupil that returns slowly to normal.

(3) Irreversible pupil dilatation with iris atrophy.

This syndrome has also been reported when no dilating drops were used.

In addition to the pupil and iris abnormalities, Urrets-Zavalia also described other features—iris ectropion, pigment dispersion, anterior subcapsular cataract and posterior synechiae. No early postoperative pressure rises were documented, although some had peripheral anterior synechiae and secondary glaucoma. Gasset also describes the glaucoma as a secondary phenomenon, commenting that it is not integral to the syndrome. In the series presented by Pouliquen et al., severe anterior uveitis, fibrinous exudate, and anterior posterior synechiae are described. An early postoperative intraocular pressure rise is documented in two of the three cases presented by Tuft and Buckley.

We describe the case of a patient undergoing deep lamellar keratoplasty for keratoconus who developed a permanently dilated pupil with iris atrophy. In addition she had marked anterior uveitis and posterior synechiae similar to the cases presented by Pouliquen et al. Dilating drops were not used.

Case report

A woman with keratoconus underwent a left deep lamellar keratoplasty at the age of 28 because of unstable contact lens fit and progressive corneal scarring. A 7.75 mm graft into a 7.5 mm diameter recipient DLK was performed under peribulbar anaesthesia with sedation. Disposable Baron Hessburg suction trephines were used and the deep lamellar dissection performed after injection of air as described by Tuft and Buckley. A paracentesis was performed and no viscoelastic or air was injected into the anterior chamber. The procedure was uncomplicated.

In her medical history of note was atopic eczema and hay fever. The eye became painful during the first postoperative evening. At the first dressing the next morning she was unable to see but the pupil was noted to be semi-dilated with an intraocular pressure of 10 mm Hg. The anterior chamber was deep and quiet.

Three weeks postoperatively, despite using topical steroids, she developed a marked anterior uveitis with posterior synechiae to the lens. This responded well to an increase in her topical steroids. However, the iris has remained fixed, dilated, and non-reactive. The visual acuity at 1 month postoperatively was 6/9+ with −1.75/−3.50 × 125.

Unfortunately 11 weeks postoperatively she developed an inferior retinal detachment. No breaks were identified but she underwent a cryobuckle procedure with an encircling band. Six months after her initial surgery she sees 6/12 wearing a contact lens correction of −2.25/−3.50 × 65. She is still troubled by glare and is somewhat unhappy with the cosmetic appearance of the eye.

Comment

The precise aetiology of this syndrome is unknown; it has been suggested that iris ischaemia can develop if it is compressed between the lens and cornea during surgery. It cannot be explained in the patients undergoing deep lamellar keratoplasty. Urrets-Zavalia syndrome has also been described after penetrating keratoplasty for other indications and after cataract surgery.

Urrets-Zavalia suggested that the strong mydriasis produced by atropine at the time of
surgery brought the iris into contact with the peripheral cornea to produce peripheral anterior synchiae and glaucoma.1 Davies and Ruben noted the condition was more common in the absence of a peripheral iridotomy and proposed a mechanism of relative pupil block.2 Naumann comments that in over 1000 cases of penetrating keratoplasty he has never seen this condition and suggests that performing a peripheral iridotomy in phakic patients is protective.3 Interestingly he always uses dilating drops.

It has been suggested that the iris is in some way abnormal in keratoconus, supported by the observation that these pupils remain dilated for longer periods following mydriasis than in normal eyes.3 Keratoconic eyes seem to hyperreact to application of mydriatics as far as speed of dilation and duration of effect, this observation is also seen the eyes of patients with Down’s syndrome.4

An abnormality of the sympathetic nervous system in the keratoconic eye remains unproven. Davies and Ruben also suggest that direct iris trauma during surgery could result in strangulation of iris vessels in the mid-periphery and ischaemic paralysis of the superior pupillae.5

Tuft and Buckley suggest in the presence of raised intraocular pressure, the low ocular rigidity of the keratoconic eye permits occlusion of the vessels at the root of iris within the sclera, which results in iris ischaemia while preserving ciliary body function.6 This case, the first to our knowledge, describes the Urrets-Zavalia syndrome following a lamellar keratoplasty. The compressive theory cannot play a part in this instance and it may lend support to the theory of an intrinsic iris abnormality in keratoconus. Equally, the pain she experienced on the first postoperative day resembles the ischaemic paralysis of the periphery and ischaemic paralysis of the iris.7

In either case, this syndrome is still poorly understood.

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Asymptomatic ocularpalatal myoclonus: an unusual case

Oculepatal myoclonus is characterised by rhythmic pendular vertical eye movements associated with synchronous contraction of the soft palate.1 It produces irritable mydriasis,2 and is normally the result of brainstem haemorrhage.3 However, it is does not usually become manifest until several months or even years later, with the longest recorded interval being 49 months.4 We present an unusual case of a patient who sustained a brainstem haemorrhage following trauma. Eight years later he was incidentally noted to have ocularpalatal myoclonus, and surprisingly was asymptomatic.

Case report

A 61 year old man was admitted to the neurosurgery department following head trauma. A computed tomography (CT) scan showed subarachnoid bleeding. An magnetic resonance image (MRI) revealed left frontal and subarachnoid bleeding. An magnetic resonance image (MRI) revealed left frontal and subarachnoid bleeding. An magnetic resonance image (MRI) revealed left frontal and subarachnoid bleeding. An magnetic resonance image (MRI) revealed left frontal and subarachnoid bleeding. An magnetic resonance image (MRI) revealed left frontal and subarachnoid bleeding.

Two weeks later he was incidentally noted to have ocularpalatal myoclonus, and surprisingly was asymptomatic.

Comment

Oculopalatal myoclonus is a rare condition normally resulting in intractable oscillopsia, thought to be caused by a lesion in the myoclonic triangle, which consists of the red nucleus, the ipsilateral inferior olive, and the contralateral dentate nucleus.7 To our knowledge, this is the first reported case of asymptomatic ocularpalatal myoclonus. It also illustrates that the latency period may be longer than that previously described.

Bilateral exudative retinopathy as the initial manifestation of retinitis pigmentsosa

A Coats’-like retinopathy affects approximately 1–4% of cases of longstanding retinitis pigmentosa (RP).1 As a presenting sign of RP, however, Coats’-like retinopathy is extremely rare.2 We present a case of bilateral exudative retinopathy suggestive of Coats’ disease in a 12 year old boy in whom investigation revealed previously undiagnosed RP.

Case report

A 12 year old male presented with a 3 week history of blurred vision in both eyes. There was no significant medical or family history. Visual acuities were 6/120 in the right eye and 6/15 in the left eye. Anterior segment examination was normal. The posterior segment of

Figure 1 (A) Fundus photograph of the right eye showing subretinal exudation, serous retinal detachment, and telangiectatic retinal vessels. (B) Fundus photograph of the left eye showing mottled granularity of the retinal pigment epithelium.
in 1956 and exudative retinopathy was first described. The association between retinitis pigmentosa and Coats'-like RP often occurs bilaterally, has no sex predisposition, and shows diffuse pigmented alterations in both eyes.

A fluorescein angiogram confirmed retinal telangiectasia, serous retinal detachment, and overlying retinal telangiectasia (Fig 1A). There was cystoid macular oedema with a lamellar macular hole in the left eye. The optic discs appeared normal. Additionally, mottled granularity of the retinal pigment epithelium (RPE) was noted in the mid-periphery of both retinas (Fig 1B). Upon further questioning, he admitted to night blindness.

A fluorescein angiogram (Fig 2A) and an electroretinogram (ERG) showed an isoelectric response under both scotopic and photopic conditions (Fig 2B). Visual field testing revealed marked constriction in both eyes. A diagnosis of retinal telangiectasia, exudative retinopathy, and retinitis pigmentosa was made and the areas of most severe telangiectasia were treated with retinal cryotherapy. One year later the retinal telangiectasia had mostly resolved, the exudation was slightly less extensive and the visual acuity was unchanged.

Comment

The association between retinitis pigmentosa and exudative retinopathy was first described in 1956 and has been termed a “Coats'-like RP.” Various studies have suggested that 1–4% of RP cases will show such a response. This entity differs from true Coats' disease in that the classic “Coats'-like” RP often occurs bilaterally, has no sex predisposition, and shows diffuse pigmented alterations in both eyes. The cause is unknown but may represent a vasodilatory response to toxic products of photoreceptor/RPE degeneration. Our case is unusual in that all previous reported cases have occurred in the setting of long-standing RP. Our patient had never consulted an ophthalmologist despite being near blind and having markedly constricted visual fields. We recommend that ophthalmologists consider an underlying diagnosis of retinitis pigmentosa in any patient presenting a picture of bilateral exudative retinopathy.

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References


Resolution of proliferative venous stasis retinopathy after carotid endarterectomy

Ocular ischaemic syndrome (OIS) may present as an asymmetric retinopathy in diabetic patients. We report a case of asymmetric diabetic retinopathy with posterior segment neovascularisation due to OIS associated with critical ipsilateral carotid stenosis where the neovascularisation resolved after carotid endarterectomy.

Case report

A 50 year old woman presented in May 1996 with left sided weakness. She had hypercholesterolaemia, hypertension, a family history of vascular disease, and was a smoker. She was found to be diabetic with peripheral retinal ischaemia and disc neovascularisation in the right eye, and minimal retinal ischaemia in the left eye (Fig 1). Her visual acuities were 6/12 in the right eye and 6/9 on the left. There was no anterior segment neovascularisation in either eye. Carotid Doppler and carotid angiography showed critical stenosis at the origin of the right internal carotid artery. The right middle cerebral artery branches were visualised as a result of retrograde flow through the ophthalmic artery. The left internal carotid artery was narrowed by 50% and there were no collaterals to the right hemisphere (Fig 2). Fluorescein angiography revealed a prolonged transit time with slow filling of choroidal and retinal vasculature, peripheral retinal capillary closure, and leakage from the disc neovascularisation.

One year later the optic disc neovascularisation and retinal ischaemia were unchanged with no iris neovascularisation. In April 1997 she underwent an uneventful right carotid endarterectomy. Two months later she developed clinically significant macular oedema in the right eye that was treated with focal argon laser photocoagulation.

Six months later the maculopathy had resolved and 14 months after surgery there was complete resolution of the optic disc neovascularisation. Three years after surgery the right eye had a visual acuity of 6/9, a near normal fluorescein angiogram transit time, minimal peripheral retinal ischaemia, and no posterior segment neovascularisation.

Figure 2  [A] Fluorescein angiogram of the right eye showing retinal ischaemia with adjacent telangiectasia. [B] Scotopic electroretinogram showing isoelectric response in both eyes.
Comment
Ocular ischaemic syndrome (OIS) is characterised in the anterior segment by flare and initial hyptony, with later iris neovascularisation. Retinopathy with neovascular proliferation occurs in the fundus because of chronic hypoperfusion. The development of neovascular glaucoma can lead to permanent blindness. In the diabetic patient OIS is superimposed on any pre-existing diabetic retinopathy, and markedly asymmetric retinopathy should prompt a search for underlying ischaemia from carotid occlusive disease. Diabetic patients with marked proliferative changes require treatment with panretinal photocoagulation (PRP), which has been shown to reduce the risk of severe visual loss and neovascular glaucoma. However, there is no clear evidence for the benefit of PRP in patients with OIS. In one study only 36% of OIS patients with iris neovascularisation responded to PRP which may be due to an ulcer rather than retinal ischaemia. In the case presented the patient was not treated with immediate PRP but reviewed regularly. The disc new vessels did not progress in the year before carotid endarterectomy and there was no immediate threat to vision.

Carotid stenosis can result in changes in the ophthalmic artery blood flow ranging from reduced antegrade to reversal of flow. If there is inadequate crossflow in the circle of Willis from the contralateral internal carotid, reversal of flow occurs in the ophthalmic artery as a consequence of a collateral circulation from branches of the external carotid artery. Although some series show no correlation between direction of flow and the severity of OIS Kerty et al in a study of 45 patients found that only reversal of flow was associated with structural changes of OIS. One similar case exists in the literature where neovascularisation resolved within several days of carotid endarterectomy (CEA). Other case reports also show that the retinopathy without neovascularisation can improve following surgery. However, the benefit of carotid endarterectomy in patients with ocular ischaemic syndrome is not quantified and it has never been shown to reverse neovascular glaucoma." The European Carotid Surgery Trial showed that the risk of ischaemic stroke in symptomatic patients with 70–99% carotid stenosis with medical treatment was only 20% over 3 years and CEAs lowered this by 30%. Based on the results of this a risk factor score suggested that a cerebral rather than an ocular event had a greater risk for stroke on medical treatment and would therefore derive greater benefit from surgery.

In the absence of iris neovascularisation and severe peripheral retinal ischaemia the ocular changes in patients with OIS can be monitored closely for the development of iris neovascularisation but the retinal vascularisation may not require early treatment with PRP.

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References

Identifying the proportion of age related macular degeneration patients who would benefit from photodynamic therapy with verteporfin (Visudyne)

Verteporfin has recently been licensed for the treatment of subfoveal exudative cases of age related macular degeneration (AMD); however, it is not clear how many patients would actually benefit from this treatment. This question has far reaching implications in terms of verteporfin’s introduction into the National Health Service in the United Kingdom.

Case report
We have recently looked at a cohort of 1418 new referrals (out of a possible 1481 (95.7%)) seen in the 166 consultant outpatient clinics at Southampton Eye Unit, between 1 December 2000 and 31 January 2001. Diagnoses were obtained from the consultant’s letter to the referring doctor following the clinic visit to obtain the spectrum of diagnoses made. When two eyes were similarly affected this was recorded as a single diagnostic event.

Cataract related diagnoses were found to be most frequent, accounting for 28.8% (397) of the total. This was followed by retinal disease at 23.4% (485).

Within the retinal disease group AMD was the single most frequent diagnosis even though it may not have been the primary reason for referral, accounting for 22.3% (108) of the 485 retinal disease cases recorded. Of the 108 AMD patients identified, 62% (67) were female and 38% (41) male, the majority being above the age of 75 (90.7%). Approximately 78% (84) of the total number of patients had AMD affecting both eyes with unilateral involvement in the remaining 22% (24).

Of the 108, most were not felt to need further investigation, having either established and untreatable disease or mild changes. Only 13% (14) underwent further investigation with fluorescein angiography. Of these, four were thought to be possibly suitable for verteporfin treatment with only one fully meeting the criteria for treatment, having a predominantly classical subfoveal membrane.

Co-existing ocular diseases such as cataract and glaucoma were treated in 49% (53) of the 108 patients, cataract extraction predominating (70% (37)).

The majority of the 107 patients (77) who did not receive verteporfin therapy did not require or were not suitable for any further assistance for their AMD. The remainder (30) were assessed for low vision aids and/or registered as partially sighted/blind.

Comment
Photodynamic therapy with verteporfin has caused much excitement, as it is heralded as a breakthrough in the treatment of exudative AMD. A recent editorial in the BMJ suggested...
that 20–30% of the 200 000 cases of exudative AMD that present to ophthalmologists each year in the United States would benefit from such photodynamic therapy.

Southampton Eye Unit serves approximately 570 000 people as part of its main catchment area, corresponding to approximately 1% of the UK population, and produced only one person over the 2 month study period suitable for treatment with verteporfin by the strict criteria for its use.1 2

The preliminary study was before the awareness of photodynamic therapy was fully developed and represents an unselected group of patients having some degree of AMD. Subsequent studies might show a higher proportion of suitable patients. One important referral is with a view for verteporfin treatment. Between August 2000 and April 2001 a total of 24 patients were assessed for verteporfin therapy resulting in seven receiving treatment, in keeping with the assessed for verteporfin therapy resulting in seven receiving treatment, in keeping with the practice guidelines. Trans Eye Vis Care Ophthalmol 2000:3–19.

A new technique for delivering sub-Tenon’s anaesthesia in ophthalmic surgery

Sub-Tenon’s local anaesthesia has become an accepted technique for anterior and posterior segment eye surgery.4 It is a safe, quick, and effective method of local anaesthesia. However, it requires a certain amount of skill for dissection into the sub-Tenon’s space. This dissection can lead to bleeding and chemosis. We describe a modification of the current technique of sub-Tenon’s anaesthesia which aims to simplify the method of local anaesthetic delivery, avoid bleeding, and chemosis while maintaining effective anaesthesia.

Case report

Fifty consecutive patients undergoing anterior segment surgery scheduled for local anaesthesia were recruited for this study. For this procedure, a 22 gauge Venflon standard intravenous cannula was used. The conjunctiva was anaesthesiﬁed with topical amethocaine 1%. A Barraquet speculum was inserted. The conjunctiva was grasped 5 mm from the limbus using toothed forceps. Under direct visualisation the tip of a 22 gauge Venflon was used to introduce the plastic cannula under the conjunctiva and Tenon’s fascia (keeping the needle tip visible at all times) (Fig 1A). The plastic cannula was advanced over the needle, which was drawn back and removed (Fig 1B). Four millilitres of lignocaine 2% with 30 international units (IU)/ml of hyaluronate was then injected through the plastic cannula (Fig 1C).

All 50 patients had anterior segment surgery. Forty-six were cataract operations with postoperative akinesia for the surgical procedure. None complained of pain. Top up of anaesthesia was non-relevant in any case. Twenty-eight patients had complete or partial ptosis. Subconjunctival haemorrhage occurring more than one quadrant occurred in one patient, but this did not interfere with surgery. None had chemosis.

Comment

Sub-Tenon’s local anaesthesia is a well established technique for ophthalmic surgery. Although the Venflon cannula does have a sharp needle, it is used simply as an introducer to place the blunt plastic cannula in the correct tissue plane. The needle tip is kept under direct visualisation at all times. Thus there is minimal risk of ocular perforation with this technique.

Venflon cannulas are used for intravenous delivery of drugs and fluid so are readily available, inexpensive, and disposable. Sub-Tenon’s cannulas in current use are specialised cannulas and therefore more costly than intravenous cannulas.

We describe a modification of the current technique of sub-Tenon’s anaesthesia which simpliﬁes the method using an intravenous cannula. We predict that this method is easier to learn and that it maintains the efﬁcacy of this type of anaesthesia without compromising safety.

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Figure 1 New technique for delivering sub-Tenon’s anaesthesia injection.
In the recent paper by Feltgen and colleagues, the intraocular pressure (IOP) was measured by Goldmann applanation tonometry and by using a cannula inserted into the anterior chamber connected with a pressure transducer. Thus, the measurement took place omitting a possible influence of the cornea on the result. Marx et al. believed that by intracamerical measurement the “true” intraocular pressure may be measured. Feltgen et al. share his opinion. They believe, therefore, that they have compared the intraoculral pressure measured with and without the possible influence of the cornea.

Feltgen et al. write in their conclusion: “There is no systematic error of applanation tonometry with increasing central corneal thickness (CCT). Therefore it is inadequate to recalculate IOP based on regression formula of applanatay IOP versus CCT.” They base their conclusion on their results. In our opinion their paper shows the following methodological deficits: (1) Both methods used for measuring IOP are not up to the demands of the scientific technique of measurement; (2) their intracamerally measured IOP values do not reflect their IOP because of bias; (3) a non-significant regression coefficient does not prove that the slope is actually 0 and, therefore, by a non-significant regression coefficient it is not proved that applanation readings are not influenced by CCT; (4) the goodness of fit of the linear regression model is insufficient; and (5) an important covariate (true IOP value) was omitted in the linear regression. We would like to discuss these points in detail.

In the study of Feltgen et al. the only criterion for the quality of measurement is the stability of the readings on the monitor. However, it is not sufficient to conclude from the presence of stability that the scale readings represent the “true” pressure value that is at the tip of the cannula. If there were a barrier inside the cannula the reading on the monitor would also be stable but would not represent the pressure at the tip. There are many pitfalls in pressure measurements by thin tubes that we know from central corneal thickness. "Minute air bubbles or tiny particles influence the result a great deal. If we want to know that a display reading represents the quantity in question then we have to conceive that the measurement system has the opportunity to react freely to changes in the quantity. This guarantee can be obtained by feeding a known signal to the input of the system and by observing the output. If the output reacts in the expected way then the guarantee is given. Ehlers et al. realised this in their rabbit experiments and we in electrophysiology.” As long as this demand is not met the results are not definitive, giving cause for criticism and leading to misinterpretations.

Feltgen et al. write in their paper (p 86): “...however we believe intracamerally measured IOP values reflect the ‘true’ IOP more accurately.” Scientific facts should not be a matter of belief. The belief of the authors in the values they measured is not justified. In the study under discussion their figure 2 shows the scatter plot of the pressure differences versus central corneal thickness. From this diagram and from their statistical calculations the authors draw their conclusions. Their results are quite different from those of Ehlers et al. They are shown here in Figures 1 and 2 on the same scale. The difference is striking.

Let’s first consider a possible reason from the physical point of view. Ehlers et al. reduced the pressure measurement to a basic physical quantity, here to the length of a water column. We can, therefore, trust the results of Ehlers et al. more than the results of Feltgen et al. who used a pressure transducer which has a zero point fluctuation up to 0.5 mm Hg (Abbott GmbH, data file). It is recommended also by the manufacturer that the zero point of the measurement system has to be determined for each patient by comparison with a water column (Dr Beer, Abbott GmbH, Wiesbaden, personal communication). This procedure is not described by Feltgen et al.

Therefore, none of the methods used in the article by Feltgen et al. may be called a reference method and all methods may be prone to error and bias. Hence, analysis of differences in IOP between these models is inappropriate in order to decide on the necessity of a conversion formula.

Further, the variability of differences is large, which is probably the result of errors in the intracameral measurement of IOP. Regression lines with a small non-significant slope (0.36 mm Hg IOP difference per 0.1 mm corneal thickness in the article by Feltgen et al. may occur in both situations where variability is both high and low. Only, in the latter case, a consequence—-the small variability—the confidence interval for the slope is narrow, may this be interpreted in the way that the covariate included in the model (that is, CCT) has no effect. If the variability is higher and the slope is approximately 0, this may lead to the conclusion that IOP measurement is inappropriate because of too large an error. This conclusion is allowed if no other essential covariates were overlooked. If variability is high and the slope of the regression line is near 0, a large p value may not be interpreted as a proof of no effect of the covariate considered in the regression model. For better interpretation of the results a confidence interval for the estimated slope should be evaluated first. If measurements by applanatary IOP are highly correlated with measurements by the reference method a correlation formula may be derived from the small linear regression. Under the assumption of small variability of residuals (difference between observed value and regression line)—that is, a satisfactory goodness of fit (for example, r²>60%), results may lead to the recommendation of the use of a conversion formula. In contrast, Feltgen et al. report an r² of 0.2%. Only for small residuals, a slope approximately 0, and a confidence interval with limits near to 0, may the recommendation that a conversion formula is not necessary be given.

Moreover, the large variability in IOP differences may occur because Feltgen et al. do not adjust for “true” intraocular hydrostatic pressure(200,645),(841,927)

References
2 Mars W, Madsjøe F, Reinhard T, et al. (More than four years experience with electronic intraocular needle tonometry) Mehr als vier Jahre Erfahrung mit der elektronischen intraokularen Nadeldruckmessung bei...

Authors’ reply

In reply to the comments of Stodtmeister and colleagues on our recent paper, we won’t argue about the correlation between central corneal thickness (CCT) and intraocular pressure (IOP), but we mistrust the clinical application of correcting factors. Stodtmeister et al compare our study to that of Ehlers et al, and we are only cited to prove an influence of corneal thickness on IOP measurement. We also confirmed these findings in our study to that of Ehlers et al, and we also cited to prove an influence of corneal thickness on the measured IOP values. In figure 2, the measurement (correlation coefficient approximated 1) is comparable to our device. We also calibrated the transducer before each measurement, and the increase of the slopes are less than 45°. We also confirmed these findings in our paper simultaneous IOP measurement on the eye of a patient with an acute eye disease (glaucoma patients requiring surgery) and cataract patients. He changed the IOP from 10 to 30 mm Hg. This method is questionable especially in glaucoma patients, because an acute IOP change could also entail endothelial alterations which could alter CCT. Unfortunately, he didn’t measure the CCT after IOP change. We have no information about the influence of IOP alterations on CCT.

In the above mentioned study authors give a hint on the influence of CCT on IOP measurement, but do not prove this assumption. It is amazing that within the last 25 years nearly 50 published papers refer to the Ehlers study without checking the results by intracameral measurement itself.

All papers measuring CCT and applanatory IOP renouncing intracameral measurement described an increasing IOP with increasing CCT. We could also confirm this finding in our study (y = 0.4 × CCT, where y is the applanatory IOP in mm Hg). Of course, it would be easiest to claim the cornea for this correlation. But it is also conceivable that with thick corneas (for example, OHT) have a reduced ocular outflow facility and consequently elevated IOP—for instance, because of a “thick” trabecular meshwork.

With the present study we tried to find out if the above mentioned correcting factors are clinically applicable at all. According to our findings they are not. We found quite variable and unpredictable differences between intraocular pressure and applanatory measurement in an individual patient. Interestingly, the same results can be found in the Ehlers study. Therefore, we renew our warning to recalibrate the IOP on central corneal thickness.

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References


NOTICES

Onchocerciasis

The latest issue of Community Eye Health (No 38) discusses onchocerciasis and the impact of interventions, with an editorial by Bjorn Thylefors, former director of the Programme for the Prevention of Blindness and Deafness, WHO. For further information please contact Community Eye Health International, Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL. (tel: +44 (0) 20 7608 6999/6910/6923; fax: +44 (0) 7250 5207; email: eyeresource@ucl.ac.uk).

Annual subscription £25. Free to workers in developing countries.

International Centre for Eye Health

The International Centre for Eye Health has published a new edition of the Standard List of Medical Equipment, Instruments and Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0) 20 7608 6910; email: eyeresource@ucl.ac.uk).

Leonhard Klein Award 2002

To promote ophthalmic surgery the Leonhard Klein Foundation bestows the Leonhard Klein Award 2002 for innovative, scientific works in the field of development and application of microsurgical instruments, as well as for microsurgical operating techniques.

The award is endowed with 15.000€ and can be conferred to an individual person as well as to a group of researchers. The prize sum must be spent for research in the field of ophthalmic surgery.

Individual and third party applications are accepted. Five copies of the works must be submitted in either English or German. The deadline for applications is 31 March 2002. Applications should be sent to: Stifterverband für die Deutsche Wissenschaft e.V., Frau Dr Marilen Macher, Postfach 164460, D-45224 Essen, Germany.

Second Sight

Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, is regularly sending volunteer surgeons to India. Details can be found at the charity website (www.secondsight.org.uk) or by contacting Dr Lucy Mathen, lucymathan@yahoo.com.

Specific Eye Conditions (SPECS)

Specific Eye Conditions (SPECS) is a not for profit organisation which acts as an umbrella organisation for support groups for any conditions or syndrome with an integral eye disorder. SPECS represents over fifty different organisations related to eye disorders ranging from conditions that are relatively common to very rare syndromes. We also include groups who offer support of a more general nature to visually impaired and blind people. Support groups meet regularly in the Boardroom at Moorfields Eye Hospital to offer support to each other, share experiences and explore new ways of working together. The web site www.eyeconditions.org.uk acts as a portal giving direct access to support groups own sites. The SPECS web page is a valuable resource for professionals and may also be of interest to people with a visual impairment or who are blind. For further details about SPECS contact: Kay Parkinson, SPECS Development Officer (tel: +44 (0)1803 524236; email: k@eyeconditions.org.uk; www.eyeconditions.org.uk).

4th International Conference on the Adjuvant Therapy of Malignant Melanoma

The 4th International Conference on the adjuvant therapy of malignant melanoma will be held on 22–24 June 2002 at the University of Essen, Germany. For further information please contact: Dr Duane C. Morrow, Department of Ophthalmology, Medical College of Wisconsin, Milwaukee, WI 53226, USA; email: dcmorrow@mcw.edu; tel: +1 (414) 955 3157; fax: +1 (414) 955 3158; www.bjophthalmol.com
be held at The Royal College of Physicians, London on 15–16 March 2002. Further details: Conference Secretariat, CCI Ltd, 2 Palmerston Court, Palmerston Way, London SW8 4AJ, UK (tel: + 44 (0) 20 7720 0600; fax: + 44 (0) 20 7720 7177; email: melanoma@confcomm.co.uk; website: www.confcomm.co.uk/Melanoma).

EUPO 2002 Course Retina
A course on retina will be held on 15–17 March 2002 at Erlangen, Germany, where European professors will teach European residents. Further details: Priv Doz Dr Ulrich Schonherr, Friedrich-Alexander-University of Erlangen-Nuemberg, Department of Ophthalmology, Schwabachanlage 6 (Kopfklinikum), D-91054 Erlangen, Germany (tel: +49 9131 853 4379; fax: +49 9131 853 4332; email: ulrich-schoenherr@augen.imed.uni-erlangen.de).

XXIXth International Congress of Ophthalmology
The XXIXth International Congress of Ophthalmology will be held on 21–25 April 2002 in Sydney, Australia. Further details: Congress Secretariat, C/- ICMS Australia Pty Ltd, GPO Box 2609, Sydney, NSW 2001, Australia (tel: +61 2 9241 1478; fax: +61 2 9251 3552; email: ophthalm@icmsaust.com.au; website: www.ophthalmology.aust.com).

12th Meeting of the European Association for the Study of Diabetic Eye Complications (EASDEC)
The 12th meeting of the EASDEC will be held on 24–26 May 2002 in Udine, Italy. The deadline for abstracts is 15 February 2002. Three travel grants for young members (less than 35 years of age at the time of the meeting) are available. For information on the travel grants, please contact Pr CD Agardh, President of EASDEC, Malmö University Hospital, SE-205 02 Malmö, Sweden (tel +46 40 33 10 16; fax: +46 40 33 73 66; email: carl-david.agardh@endo.mas.lu.se). Further details: NORD EST CONGRESSI, Via Aquilea, 21–33100 Undine, Italy (tel: +30 0432 21391; fax: +39 0432 50687; email: nordest.congressi@ud.nettuno.it)

International Society for Behçet’s Disease
The 10th International Congress on Behçet’s Disease will be held in Berlin 27–29 June 2002. Further details: Professor Ch Zouboulis (email: zoubbere@zedat.fu-berlin.de).

Singapore National Eye Centre 5th International Meeting
The Singapore National Eye Centre 5th International Meeting will be held on 3–5 August 2002 in Singapore. Further details: Ms Amy Lim, Organising Secretariat, Singapore National Eye Centre, 11 Third Hospital Avenue, Singapore 168751 (tel: (65) 322 8374; fax: (65) 227 7290; email: Amy_Lim@snec.com.sg).

CORRECTION
We regret that an error occurred in the mailbox letter published by Kenawy et al in the November 2001 issue of BJO (2001;85:1394–5). The name of one of the authors was incorrect and should have been Omar M Ayoub.
Identifying the proportion of age related macular degeneration patients who would benefit from photodynamic therapy with verteporfin (Visudyne)

N Mandal and I H Chisholm

*Br J Ophthalmol* 2002 86: 118-119
doi: 10.1136/bjo.86.1.118

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