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AT1-RECEPTOR-BLOCKADE AND AT2-RECEPTOR-STIMULATION ACT TISSUE-PROTECTIVE IN EXPERIMENTAL DIABETIC RETINOPATHY

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Purpose. This study analysed the effect of pharmacological interference with the renin-angiotensin-system by either AT1-receptor (AT1R) blockade with Candesartan or by AT2-receptor (AT2R) stimulation with the novel non-peptide AT2R-agonist, Compound 21 (C21) on diabetic retinopathy in hypertensive rats.
Methods. Animals rendered diabetic by streptozotocin (i.v.) were treated orally for 8 weeks according to the following protocol: 1) non-diabetic controls (CON); 2) diabetic controls (STZ); 3) STZ+ blood-pressure (BP) lowering dose of Candesartan (7.5mg/kg BW/d) (STZ+Cand7.5); 4) STZ+ non-BP-lowering dose of Candesartan (0.2mg/kg BW/d) (STZ+Cand0.2); 5) STZ+C21 (0.3mg/kg BW/d); 6) STZ+Cand7.5+C21. BP was measured every second week. Retinas were analysed for mRNA levels of neurotrophins and apoptosis markers.
Results. Systolic BP was lowered in the STZ+Can7.5 (168.5±20mmHg), and the STZ+Cand7.5+C21 (145±35 mmHg) groups, but not in the STZ+Cand0.2 (197.5±15 mmHg) and, remarkably, not by AT2R-stimulation in the STZ+C21 (191±38mmHg) group. AT2R-stimulation and AT1R-blockade significantly increased neurotrophin (BDNF) and neurotrophin receptor (TrkB) expression. The apoptotic markers Caspase-3 and BAX/Bcl2 ratio were significantly decreased by both treatment strategies. AT1R-blockade and AT2R-stimulation acted tissue protective independently of BP reduction.
Conclusions. We conclude that pharmacological intervention with the RAS by AT1-receptor blockade or AT2-receptor stimulation ameliorates experimental diabetic retinopathy acting tissue-protective and anti-apoptotic in a BP-independent way. Our results provide a potential molecular mechanism for the reduced incidence in diabetic retinopathy in normotensive type-1 diabetic patients by Candesartan treatment observed in the recently published DIRECT study.

INTRACELLULAR SIGNALING PATHWAY INVOLVED IN TNF-α-INDUCED ACTIVITY OF CORE 2 GLCNAC-T IN DIABETIC LEUKOCYTES

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Purpose. To explore NADPH oxidase signalling pathway in tumour necrosis factor-alpha (TNF-α)-induced activity of core 2 GlcNAc-T (Ben-Mahmud et al, 2006) in diabetic leukocytes.
Methods. Human leukocytes (U937 cells) and Epstein-Barr–transformed lymphoblastoid cell lines with different gene copies of p47phox (major subunit of NADPH oxidase) were cultured in RPMI medium containing normal (5.6mM) glucose and used for the study. Cells were exposed to TNF-α (8pg/ml) for 24h in the presence and absence of (i) NADPH oxidase inhibitors (30μM apocynin and 1μM scrambled and unscrambled gp91ds-tat), (ii) LY379196 (specific PKC-β 1/2 inhibitor, 50nM) and (iii) antioxidants N-acetyl cysteine (NAC, 15mM) and Tiron (5mM). NADPH oxidase activity was measured using cytochrome C reduction assay. PKC-β 1/2 activity was measured using TruLight™ PKC-β 1/2 assay kit.
Results. Compared to control medium, exposure to TNF-α raised core 2 GlcNAc-T activity in human leukocytes

[1722±255.3 (n=10) vs. 374±80.3 (n=10), p<0.0001] that was significantly reversed with apocynin and LY379196. These findings were supported using gp91ds-tat (scrambled and unscrambled), a specific NADPH oxidase inhibitor, and lymphoblastoid cell-line deficient in p47phox, and reversal with NAC and Tiron.
Conclusions. Our results demonstrate a novel signalling crosstalk between TNF-α, core 2 GlcNAc-T, NADPH oxidase and PKC-β 1/2 in diabetic leukocytes.

IMPAIRMENT OF AUTOREGULATION IN MACULAR AND PERIPHERAL RETINAL ARTERIOLES IN DIABETIC RETINOPATHY

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Purpose. We therefore compared the diameter response of macular and peripheral arterioles in diabetic patients with maculopathy (D-MAC) or proliferative retinopathy (PDR) after an increase in the arterial blood pressure induced by isometric exercise.
Methods. Twenty-four diabetic patients (mean age 49.8 years, range 31-75 years) were examined of which seventeen had D-MAC and seven had PDR. Using a Retinal Vessel Analyzer (RVA) the diameter response of a macular and a peripheral arteriole located within four-disk diameters of the optic disk was recorded in each person before and after increasing the blood pressure by lifting a 2 kg hand weight.
Results. There was no significant difference between the baseline diameter of the studied macular (97.3±2.4) and peripheral (93.7±3.0) arterioles (p=0.34). Lifting the hand weight increased the arterial blood pressure by 27.1±3.8 mmHg (D-MAC) and 18.7±6.1 mmHg (PDR). The increased blood pressure induced no significant change in the diameter of macular arterioles in neither D-MAC patients (-0.09%±0.76%, p=0.97), nor in PDR patients (-0.96%±2.4%, p=0.72). However, the diameter of the peripheral arterioles decreased significantly in D-MAC patients (-1.96±0.68%, p=0.01) and increased non-significantly in PDR patients (+4.00±2.33) (p=0.20).
Conclusions. Autoregulation in arterioles supplying the retinal periphery differs among diabetic patients with maculopathy and patients with proliferative retinopathy. The findings may help explain the different responses in the macular area and the retinal periphery in the two retinopathy complications.

THIAMINE AND BENFOTIAMINE COUNTER APOPTOSIS INDUCED BY INTERMITTENT HIGH GLUCOSE EXPOSURE IN HUMAN RETINAL PERICYTES

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Purpose. Our aim was to verify if thiamine and benfotiamine are able to counter intermittent high glucose-induced damage in HRP.
Methods. Wild-type and immortalized pericytes were kept intermittently at 48h intervals in high/normal glucose for 8 days, with or without the addition of 50 or 100 µmol/L thiamine or benfotiamine. Control cells were cultured in stable physiological or high glucose for the whole period. DNA fragmentation, Bcl-2 and Bax mRNA expression and protein concentration, as markers of glucose-induced apoptosis, were determined.
Results. Intermittent, but not stable, exposure to high glucose increased apoptosis in both types of HRP. Thiamine and benfotiamine were able to counter this damaging effect, when added to intermittent high glucose samples. Bcl-2/Bax expression/concentration results were consistent with DNA fragmentation.
Conclusions. The hypothesis that daily blood glucose fluctuations play a major role in the development of diabetic retinopathy is reinforced by the confirmation that apoptosis in human pericytes is increased following intermittent high glucose exposure only. Thiamine and benfotiamine are able to prevent pericyte apoptosis, suggesting once again that this vitamin could be an inexpensive approach to the prevention and/or treatment of diabetic vascular complications.

DIFFERENTIAL TGF-BETA SIGNALING PATHWAYS IN RETINAL ENDOTHELIAL CELLS AND PERICYTES

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Purpose. Our aim is to investigate TGF-beta signalling in retinal vascular cells.
Methods. Bovine retinal endothelial cells (BRECs) and pericytes (BRPCs) were stimulated with different concentrations of TGF-beta with or without a specific TGF-beta type I receptor-inhibitor, SD-208. To determine TGF-beta-signalling activity, western blotting was used to detect phosphorylated Smad2 protein at different time points. Qualitative RT-PCR was performed to compare gene expression levels of TGF-beta receptors and determine the effect of TGF-beta on profibrotic gene expression (PAI-1, fibronectin and CTGF) in endothelial cells and pericytes.
Results. ALK5 was equally expressed in both cell types, whereas endoglin and TGF-beta receptor-II were preferentially expressed in BRECs. ALK1 was expressed in BRECs only. In

BRECs, TGF-beta dose-dependently induced phospho-Smad2 protein, which was efficiently blocked by SD-208. In contrast, in pericytes, TGF-beta induced phospho-Smad2 protein already at low concentration which could be blocked by SD-208. TGF-beta caused up-regulation of downstream pro-fibrotic genes PAI-1 and fibronectin in both cell types, which was prevented by SD-208. However, CTGF mRNA expression was only induced by TGF-beta and inhibited by SD-208 in BRPCs.
Conclusions. TGF-beta induces Smad2-phosphorylation in bovine retinal vascular cells through the TGF-beta type I receptor, especially in pericytes, which leads to increased expression of pro-fibrotic genes. This suggests that the pro-fibrotic gene expression observed in DR may be caused by TGF-beta, which may serve as an intervention target.

MICROANEURYSMS FORMATION RATE AS A PREDICTOR OF DR PROGRESSION TO CSME NEEDING PHOTOCOAGULATION IN NONPROLIFERATIVE RETINOPATHY IN DIABETES TYPE 2

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Purpose. To examine the relation between microaneurysms (MA) formation rate using a new semi-automatic method based on colour fundus photographs, and DR progression.
Methods. Ninety-five patients/eyes with type 2 diabetes and nonproliferative retinopathy were followed-up for 2 years with ophthalmological examinations every 6 months, including stereoscopic colour fundus photography and were maintained under good metabolic control. All patients were followed-up for the following 8 years by conventional general and ophthalmological care accomplishing a total 10 years follow-up. Photocoagulation for CSME was considered as the study main endpoint. Using a new semi-automatic method for MA earmarking, which takes into account the exact location of each MA, the MA formation rate for the first 2 years of follow-up was assessed (number of new MA appearing per year).
Results. At the end of the 10-year period of follow-up, 16 of the 95 patients had developed CSME needing photocoagulation. A MA formation rate of 8.01±0.0 MA/year (mean±SD) was found in these 16 patients' eyes, being it statistically higher than for patients' eyes that did not develop CSME (mean±SD: 1.8±2.3) (p=0.003).
Conclusions. A high MA formation rate earmarked on colour fundus photographs appears to be a good predictor of DR progression to CSME needing photocoagulation in type 2 diabetic patients with nonproliferative retinopathy.

DIABETIC RETINOPATHY IN A COHORT OF PREGNANT WOMEN FROM SOUTHERN DENMARK

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Purpose. To describe the prevalence and progression of retinopathy in women with diabetes examined at a photographic screening clinic during and after pregnancy.
Methods. Pregnant women with diabetes from Southern Denmark (1,2 mill. inhabitants) were included. Fundus photographs were taken in each trimester, post partum and yearly thereafter. Retinopathy was graded according to the EURODIAB protocol.
Results. 132 women were examined at least once during pregnancy from January 1997 to April 2003 and thereafter until January 2009. Median age at first examination was 29 years (range 19-42), median duration 10 years (0-36) and median HbA1c 6.8% (4.6-10.3). At baseline 34 patients had mild nonproliferative retinopathy, 8 had severe nonproliferative retinopathy and 8 women had proliferative retinopathy. Six patients (4.5%) developed mild nonproliferative retinopathy during pregnancy and 10 (7.6%) progressed (one to proliferative retinopathy). The patients were followed for 6.2 (± 3.6) years after the pregnancy. Within 3 months post partum 10 patients (4.5%) developed or progressed in retinopathy. After 6 years of follow-up 11 patients had developed retinopathy and 36 patients had progressed in retinopathy in one or both eyes (8 to proliferative retinopathy). Risk factors for progression and PDR will be presented.
Conclusions. The incidence and progression of retinopathy during pregnancy and soon after delivery was considerable (19.7%). A few patients progress to sight threatening retinopathy. Diabetic women should be examined regularly before, under, as well as after pregnancy. Particular attention should be given to screening after pregnancy completion.

REFERRALS FROM DIABETIC RETINOPATHY SCREENING WITH "MACULOPATHY": 18 MONTH FOLLOW-UP

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Purpose. To provide information that may help to refine screening criteria regarding photographic diagnosis of maculopathy and prioritise referrals.
Methods. Clinical data were recorded from 90 patients with M2 seen in the diabetic eye clinic over a 6-month period in 2007 and repeated from clinical examinations 18-24 months later.
Results. 53 patients (91% of patients) with M2HEx had follow-up data available. A further 20% of patients required macula laser treatment in the follow-up period. 66% required continued review. 29 patients (91%) with M2Hg had follow-

up data available. 1 patient required macula laser treatment in the follow-up period. 77% required continued review.
Conclusions. The majority of referrals continue to require long-term follow-up with significant implications for diabetic eye clinics. 40% of patients with M2HEx require laser treatment within 2 years suggesting that this is a high risk group. This information is useful for prioritising referrals from diabetic retinopathy screening programmes and refining referral criteria.

A LARGE SCALE VALIDATION OF AUTOMATED GRADING

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Purpose. To evaluate the performance of combined automated image quality assessment and automated microaneurysm detection on a large multi-centre unselected data set.
Methods. Images and grading results from 36069 anonymised patient screening episodes were obtained from two screening centres. Photography and grading had been performed according to the Scottish screening recommendations. Automated image quality and automated "disease/no disease" detection were performed. The detection rate of the automated system was evaluated for each retinopathy grade as assigned by the screening programmes.
Results. According to the manual grades, the automated system detected: image quality failures 98.17% (1877/1912), referable maculopathy 95.79% (1183/1235), referable background retinopathy 99.13% (337/340), and proliferative retinopathy 99.04% (206/208). Automated grading provided a final grade for 36.4% of all screening episodes.
Conclusions. Automated grading reduces the manual grading working whilst achieving a high sensitivity for the detection of referable retinopathy/maculopathy in a large multi-centre unselected data set.

DIABETES AND ASYMPTOMATIC RETINAL EMBOLI

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Purpose. To determine outcome and risk factor data for diabetic patients with asymptomatic emboli.
Methods. A retrospective analysis of images and cases notes between November 2001 and November 2008.
Results. 216 people were identified with asymptomatic emboli, 69% men, 31% women, of whom 82.9% are alive and 17.1% have died. The median age of 73 years was older than the general screening population ($p<0.0001$), minimum 52, maximum 93, interquartile range 66 to 78 (mean 72.5, standard deviation 8.7). The median follow-up was 2 years, maximum 7 years. The proportion who had died since emboli were identified was 8%, 14%, 20% and 25% at 1, 2, 3 and 4 years respectively. The embolus was in the right eye in 53.5% in the left in 46.5% ($p=0.30$ for equal proportions). The location was 44.5% supero-temporal, 41.6% infero-temporal, 3.3% a combination of the above, 6.7% supero-nasal, 3.3% infero-nasal and 0.5% in a naso ciliary vessel. 16.3% were calcific, 79.8% cholesterol and 3.9% fibrinoplatelet. The clinical notes review shows the following preliminary data: HbA1c median 6.9, interquartile range 6.4 to 7.5. The proportion with <50%, 50-60% and >70% ipsilateral internal carotid artery stenosis is 67%, 15%, 18%, and contralateral 76%, 21%, 3%.
Conclusions. There is a high mortality associated with asymptomatic emboli. More detailed analysis will add to the evidence base for study design to improve the outcome for these patients.

HIGH GLUCOSE-CONDITIONED MEDIUM FROM ENDOTHELIAL CELLS ENHANCES APOPTOSIS IN HUMAN RETINAL PERICYTES

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Purpose. We aimed at evaluating human retinal pericyte (HRP) response to soluble factors released by Human Umbilical Vein EC (HUVEC) in the presence of physiological or high glucose in the medium.
Methods. EC were cultured in physiological or high glucose for 7 days; media from the last 2 days of culture were collected and filtered (HUVEC-CM). HRP were cultured for 7 days in normal/high glucose, or in normal glucose with the addition of 25/50% HUVEC-CM. DNA fragmentation was measured by ELISA, Bax and Bcl-2 mRNA expression by RT-PCR and HRP morphology by phase-contrast microscopy.
Results. Apoptosis increased significantly in the presence of 50% HUVEC-CM produced in high glucose, but not in high glucose only, nor with HUVEC-CM produced in normal glucose. In terms of mRNA expression, there was clear over-expression of Bax and an evident reduction of Bcl-2 in the presence of 50% HUVEC-CM produced in high glucose. Cell morphology showed modifications in the presence of 50% HUVEC-CM produced in high glucose.
Conclusions. HRP apoptosis increases significantly in the presence of conditioned-medium from HUVEC cultured in high glucose, but not in other conditions, suggesting that soluble factors derived from EC are likely to play a critical role in the apoptotic response of HRP.

DIABETIC MACULAR EDEMA: MULTIMODAL IMAGING

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Purpose. The aim of this study was to evaluate the role of structural and functional macular imaging in the characterization of DME patterns.
Methods. One hundred twenty-five eyes of 78 diabetic patients with untreated DME underwent: best corrected visual acuity determination (BCVA, logMAR), slit lamp biomicroscopy, fluorescein angiography, OCT [mean central field (CF) retinal thickness, volume and DME pattern], fundus autofluorescence (FAF): absent or increased FAF (IFAF: single and multiple spots; IFAF area quantification), retro-mode scanning laser ophthalmoscopy and microperimetry.
Results. Thirty-five eyes had normal FAF, 90 IFAF (30 single spot IFAF, 60 multiple spots IFAF). Retinal sensitivity over areas with IFAF was 10.8 dB (vs 16.2 db in normal areas, $p<0.005$). Retinal sensitivity of the CF vs FAF was: 14.6 dB normal FAF, 12.10 dB single spot and 10.9 dB multiple spots IFAF ($p<0.05$). A significant correlation was found between IFAF, CF retinal sensitivity and positive retro-mode imaging ($p=0.01$). Cystoid OCT-pattern and macular volume were correlated to both presence and dimension of IFAF and retro-mode imaging ($p<0.05$), whereas sponge-like and subfoveal neuroretinal detachment were not correlated. BCVA did not correlate either to FAF pattern or area of IFAF.
Conclusions. The use of an integrated structural and functional retinal imaging approach allows to identify some different DME phenotypes, which may be related to treatment prognosis when prospectively evaluated.

ACTIVE HIF-1α IN THE NORMAL HUMAN RETINA

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Purpose. We hypothesize that HIF-1α is constitutively stabilized and active in the normal human retina.
Methods. The cellular distribution of HIF-1α and the expression of its downstream targets vascular endothelial growth factor (VEGF), glucose transporter 1 (GLUT-1) and carbonic anhydrase IX (CAIX) were investigated by immunohistochemistry and immunoblotting in the retina of normal human donor eyes and in perfusion-fixed rat retina.
Results. Both human and rat retina displayed prominent staining of HIF-1α in nuclei of most cell types in inner and outer nuclear layers and the ganglion cell layer, a cellular distribution which was confirmed in human retina by western blotting of nuclear extracts. In the human retinas, specific cell types stained for VEGF, GLUT-1 and CAIX.
Conclusions. Our observations indicate that active HIF-1α signalling occurs constitutively in the normal human and rat retina, suggesting that HIF-1α has a physiological role in the retina.

DIGITAL RETINAL SCREENING FOR DIABETIC RETINOPATHY IN ETHIOPIA: THE LEOPARD PROGRAMME

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Purpose. The aim is to establish whether digital photographic retinal screening for diabetic retinopathy (DR) is sustainable and worthwhile.
Methods. Similar technology and protocols to the English DR screening programme have been introduced into the Black Lions Diabetes Centre (BLDC) (approximately 2000 diabetics, 300 outpatient attendances per month). Primary grading was performed by trained staff in the BLDC. All photographs were rechecked for quality assurance (QA) by HEDRSC graders.
Results. During the first year, a total of 493 diabetic patients completed the screening protocol (47% male, 51% female, mean age 47 years, range 8 to 78). 33/493 (7%) patients had best binocular visual acuity (VA) of 6/60 or worse. Final grading showed that 190/493 (39%) patients had no DR and 58/493 (12%) had ungradable image sets. Retinopathy status in the remainder (49% of total) was background 17%, preproliferative 7%, proliferative 4 % and 28% (n=138) had referrable maculopathy. Inter-grader agreement between BLDC and HEDRSC was 92% for those returned to annual screening, 69% for those requiring urgent referral, and 98% for specifically identifying sight-threatening DR for referral.
Conclusions. After 18 months screening, the digital camera technology employed is sustainable, and the BLDC trained staff have achieved accurate identification and referral for sight-threatening DR.

RETINOPATHY AND NEPHROPATHY RISK IN SUBJECTS WITH HIGH GLYCATION: THE HOORN STUDY

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Purpose. To explore the association of glycation with retinopathy and nephropathy.
Methods. Ten-year follow-up data of a glucose status stratified sample (n = 631, age 50-75) of the Hoorn Study, a popu-

lation-based cohort, were used. Odds ratios from logistic regression analysis were computed for three categories of HbA1c with three levels of fasting glucose (FG) and with the category of low HbA1c and low FG as a reference. Within each subgroup of FG (≤6 mmol/L, 6-7 mmol/L and >7 mmol/L) subjects with HbA1c >6% were considered high glycators. Furthermore, a measure of glycation, the glycation gap, observed HbA1c minus HbA1c corrected for fructosamine, was analysed in tertiles. Retinopathy incidence was assessed by fundus photography in n=233, nephropathy was estimated by the Cockcroft-Gault formulas in n=221.
Results. The crude odds ratios for retinopathy were 37.0 (95% CI: 2.3-602.7), 44.4 (4.4-49.0) and 9.3 (1.1-81.7) for high glycators with low, intermediate and high FG levels, respectively. Gender, age and hypertension did only slightly attenuate these associations. The highest glycation gap tertile showed a crude odds ratio of 2.1 (95% CI: 0.7-6.5) for retinopathy compared to the lowest tertile. Results on nephropathy were statistically non significant.
Conclusions. Elevated HbA1c predicts retinopathy, but not nephropathy, also in subjects with low fasting glucose levels.

PREVALENCE AND 25-YEAR INCIDENCE OF PROLIFERATIVE RETINOPATHY AMONG DANISH TYPE 1 DIABETIC PATIENTS

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Purpose. To evaluate the prevalence of retinopathy among long-time surviving type 1 diabetic patients as well as the 25-year incidence of proliferative retinopathy and associated risk factors in a Danish population-based cohort.
Methods. A population-based cohort of 727 type 1 diabetic patients from Fyn County, Denmark, was identified in 1973. In 1981-82, baseline retinopathy was graded and other risk factors were assessed in 573 patients. Twenty-five years later, 308 patients were still alive. Of these, 201 (65.3%) were re-examined at follow-up in 2007-08.
Results. Median age and duration of diabetes at follow-up were 58.8 and 43 years, respectively. At follow-up, the prevalence of any retinopathy was 96.9%. Non-proliferative retinopathy was found in 47.9%, and 49.0% had proliferative retinopathy. The 25-year incidence of proliferative retinopathy was 41.1% among patients at risk. In multivariate analyses, baseline HbA1 (OR 2.26 per 1% increase, 95% CI: 1.08-4.72) and non-proliferative retinopathy (OR 4.96, 95% CI: 2.00-12.3) were the only risk factors for incident proliferative retinopathy. The long-term incidence of proliferative retinopathy was not associated with baseline duration of diabetes, proteinuria, smoking, BMI, maculopathy, systolic or diastolic blood pressure.
Conclusions. Retinopathy among long-term surviving type 1 diabetic patients is almost universal. Proliferative retinopathy was found in half of these patients. Additionally, the 25-year incidence of proliferative retinopathy was high. Baseline glycaemic regulation and non-proliferative retinopathy were identified as risk factors for incident proliferative retinopathy.

Poster Session

RETINAL OVEREXPRESSION OF ANGIOPOIETIN-2 MIMICS DIABETIC RETINOPATHY AND ENHANCES VASCULAR DAMAGES IN HYPERGLYCAEMIA

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Purpose. In this study, we investigated the effect of retinal overexpression of human Ang2 (mOpsinhAng2 mouse) on vascular morphology in non-diabetic and streptozotozin-induced diabetic animals.
Methods. Pericyte (PC) coverage and acellular capillary (AC) formation were quantitated in retinal digest preparations after 3 and 6 months of diabetes duration.
Results. The degree of retinopathy in non-diabetic mOpsinh-Ang2 mice at 3 months (-21% PC, +49% AC) was comparable to age-matched diabetic wild type mice. Diabetic mOpsinhAng2 mice exhibited significantly worse vascular pathology than wild type counterparts at 6 months. Quantitative PCR revealed that human Ang-2 mRNA was highly overexpressed in retinas of transgenic mice.
Conclusions. Our data demonstrate that overexpression of Ang-2 in the retina enhances vascular pathology, indicating that Ang-2 plays an essential role in diabetic vasoregression via destabilization of pericytes.

IDENTIFICATION OF PERIVASCULAR CELLS IN RETINAL ARTERIOLES WITH A POTENTIAL ROLE FOR THE PATHOPHYSIOLOGY OF DIABETIC RETINOPATHY

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Purpose. It has been shown that the vasodilating effect of ATP, but not adenosine, depends on the perivascular retinal tissue, but the factors responsible for this effect in the perivascular retina are unknown.
Methods. Porcine retinal arterioles with surrounding retina were mounted in a wire myograph and placed in a confocal microscope and loaded with a calcium sensitive fluorophore allowing simultaneous recording of vascular tone and calcium activity. The vascular tone and changes in calcium activity in the perivascular cells were studied after addtion of increasing concentrations of adenosine and ATP.
Results. Both adenosine and ATP reduced the tone of the retinal arterioles ($p=0.05$) and the activity of intracellular calcium in vascular smooth muscle cells significantly ($p=0.01$). However, ATP ($p=0.01$), but not adenosine, increased the calcium activity in perivascular cells located on the lateral aspects of the arterioles and immediately external to the vascular smooth cells.
Conclusions. Perivascular retinal cells participate in the regulation of retinal vascular tone through mechanisms that involve ATP. Adenosine produced by degradation from ATP induces vasodilation by a direct effect on retinal vascular smooth muscle cells. This may contribute to a better understanding of diseases where the regulation of the blood flow is disturbed, such as diabetic retinopathy.

L-GLUTAMIC ACID RELAXES PORCINE RETINAL ARTERIOLES THROUGH A NMDA RECEPTOR DEPENDENT MECHANISM THAT MIGHT BE INVOLVED IN VASCULAR FLOW DISTURBANCES OF DIABETIC RETINOPATHY

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Purpose. To study the interaction between glutamate signalling in the retina mediated by different glutamate receptors, and the resulting vasodilation of retinal arterioles.
Methods. Porcine retina-surrounded arterioles were mounted in a wire myograph for isometric force measurements. After pre-constriction of the arterioles, the vasorelaxing effects of L-glutamic-acid combined with antagonists to respectively the NMDA-, metabotropic, and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic-acid (AMPA)-/kinate glutamate receptors were studied. Each experiment was repeated after removal of the retinal tissue.
Results. L-glutamic acid induced a dose-dependent vasorelaxation, $p<0.001$ repeated measures ANOVA, ($EC50=118.62$ μM), which disappeared when the retina was removed. The NMDA-antagonist, DL-APV, but not antagonists to metabotropic (MCPG) nor the AMPA/kinate receptors (CNQX), caused a significant reduction of L-glutamic-acid induced vasorelaxation ($p=0.033$, $p\geq0.1$ and $p\geq0.11$, respectively).
Conclusions. The vasorelaxation of L-glutamic-acid on preconstricted porcine retinal arterioles depends on the perivascular retina and is mediated through NMDA, but not metabotropic or AMPA/kinate receptors. The findings contribute to the understanding of the tone regulation of retinal arterioles, and may help identify mechanisms impaired in retinal vascular disease, such as diabetic retinopathy.

RETINAL VESSEL OXIMETRY USING HYPERSPECTRAL IMAGING IN DIABETIC RETINOPATHY

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Purpose. To demonstrate the techniques of measuring oxygen saturation in the retinal vasculature in subjects with proliferative diabetic retinopathy.
Methods. High resolution en face hyperspectral retinal images were acquired using a modified conventional fundus camera. 3 subjects with proliferative diabetic retinopathy were examined prior to pan-retinal photocoagulation. Algorithms incorporating physical optics models for light propagation within the retina were used to calculate the blood oxygen saturation along the larger retinal blood vessels.
Results. Our oximetry analysis techniques were capable of generating oximetric maps of the retinal vasculature. In subjects with proliferative diabetic retinopathy, the oxygen saturation in a number of retinal venules adjacent to the new vessels was significantly higher than normal.
Conclusions. Hyperspectral imaging in subjects with diabetic retinopathy has the potential to detect abnormal oxygen saturation within the retinal circulation. The increased venular oxygen saturation in the diabetic retina suggests either a reduced metabolic demand for oxygen in the retinal tissues or an arterio-venous shunting phenomenon within the retinal circulation. Further improvements in the analysis algorithms could enable the measurement of oxygen saturation in the retinal capillaries. These techniques may be applied to the detection and monitoring of disease progression in patients with diabetic retinopathy.

SEGMENTATION OF FOVEAL AVASCULAR ZONE FROM FLUORESCEIN ANGIOGRAPHY USING A LEVEL SET METHOD

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Purpose. To investigate the feasibility and reliability of the level set method to segment the foveal avascular zone (FAZ) on fluorescein angiogram (FA) images.
Methods. High-resolution FA sequences were acquired on HRA2 (Heidelberg Engineering, Germany) in patients with reasonable media clarity (LOCS score ≤2). A single transit-phase frame was selected and analysed. A sub-image containing the FAZ was cropped from the original and smoothed with a Gaussian kernel (σ=1.5). An initialising contour was manually placed within the FAZ of the smoothed image and was iteratively driven by the level set method towards the FAZ boundary. To evaluate the repeatability an average overlap ratio of area Ra (intersection/union) over 10 segmentations with different initialisations was obtained for each of the images.
Results. Images from 19 patients were studied. Visual inspection showed segmentation on 11 images with reasonable clarity of FAZ produced satisfactory accuracy with good repeatability [mean (±SD) of Ra: 97.2% (±2.8%)]. The remaining 8 images had poorer image quality due to poor patient co-operation and other pathologies and their segmentation results suffered with a lower repeatability [mean (±SD) of Ra: 53.1% (±30.7%)].
Conclusions. The proposed segmentation approach shows promising results for automated segmentation of the FAZ. Further optimisations on data acquisition and image enhancement are under investigation for its introduction into general clinical practice.

"THESE IMAGES THAT YET FRESH IMAGES BEGET"

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Purpose. Evaluation of an automated grading system employed as part of a diabetic retinopathy screening program.
Methods. Comparison of primary manual and automated digital image assessment with arbitration of discrepancies by an experienced grader and an ophthalmologist.
Results. A total of 530 cases were included in the analysis. Outcomes from the automated process were as follows; 88 (16.5%) were unassessable, 252 (47.5%) disease negative and 190 (36%) disease positive. For the manual grading process 12 (2.2%) cases were unassessable, 363 (68.5%) disease negative and 155 (29.3%) disease positive. 6 cases graded as unassessable by the manual grader were passed as assessable and disease negative by the automated process. After arbitration a single disease positive case – featuring one cotton wool spot – was identified in this group. 7 cases graded as disease positive by the manual process were graded as disease negative by the automated process. After arbitration no disease positive cases were identified in this group. Use of the automated process for level one grading resulted in a grading workload reduction of 47.5%. Application of automated grading shortened the grading turnaround by avoiding manual grader backlog and delivered a 40% saving compared with previous costs.
Conclusions. Automated grading resulted in a clinical discrepancy rate of 0.2% (1/530). Arbitration by experienced graders concluded that this case did not constitute a true clinical risk. Automated grading provides a safe, time-saving, cost-effective alternative to manual level one grading.

AGREEMENT BETWEEN PHOTOGRAPHIC AND HOSPITAL BIOMICROSCOPY GRADING OF DIABETIC RETINOPATHY

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Purpose. To compare agreement between grading of photographs in a screening service and hospital biomicroscopy grading using the UK NSC classification.
Methods. A hospital EMR (Medisoft) was routinely used to force a structured assessment of clinical signs of diabetic retinopathy and automatically calculate the grade according to the NSC. This was compared with the grading at screening.
Results. Data on 226 patients (452 eyes) referred in 2006-2007 were analyzed. Screening retinopathy grades were: R0, 44; R1, 278; R2, 182 and R3, 12 eyes. Biomicroscopy grades agreed in 348 eyes (76.9%), showed a higher grade in 60 and a lower grade in 44 eyes (kappa = 0.59). The commonest reason for disagreement was screening overgrading R1 (background retinopathy). Screening maculopathy grades were: M0, 250 and M1, 202 eyes. Biomicroscopy grades were in agreement in 328 (72.6%), showed a higher grading in 120 and a lower grade in 4 eyes (kappa = 0.41). The commonest cause for disagreement was clinicians failing to identify exudates.
Conclusions. This study establishes benchmark standards for agreement between screening services and hospital eye departments.

REVIEW OF PATIENTS IN TOWER HAMLETS WITH POOR VISION RECORDED IN DIABETIC RETINOPATHY SCREENING

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Purpose. This study analysed causes of low vision and related care in Tower Hamlets (TH) Diabetic Retinopathy (DR) Screening Programme.

Methods. Systematic screening has been offered in TH since 10/2002. In 7/2008, all patients with 6/60 or 6/24 or worse vision in both eyes (UK blind and partially sighted registration levels respectively) had their screening and hospital records audited. The TH Low Vision Services (THLVS) audited their records for these patients, and then for all with diabetes related blindness registered on their database.

Results. In screening, 46 patients had visual acuity levels of blind and 140 patients of PS registration. Less than 10% of these patients had DR related visual loss, the rest were caused by cataract, other retinal diseases and cerebrovascular incidents. On THLSV records 25 patients were found to have DR recorded, all of these were in the appropriate screening pathway. However, THLSV was unaware of the majority of patients who had non-diabetes related sight problems.

Conclusions. Screening for DR finds all causes of visual loss, thus in order to have a major impact on the population as a whole, a systematic approach coupled with targeted care and educational actions is needed to deal with the impact of low vision on society.

INTER-GRADER AGREEMENT IN THE BRISTOL AND WESTON DIABETIC RETINOPATHY SCREENING PROGRAMME: AN INTERNAL QUALITY ASSURANCE AUDIT

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Purpose. To determine the accuracy of primary graders in the Bristol and Weston diabetic retinopathy screening programme in identifying referable retinopathy, non-referable retinopathy and un-gradable disease.

Methods. A prospective audit of image sets from 6 fully trained primary graders in the Bristol and Weston diabetic retinopathy screening programme was carried out between June and July 2008. 100% of all images graded both disease-positive and disease-negative by the primary graders were re-graded by an expert grader blinded to the primary grading results. The level of inter-grader agreement between primary graders and the blinded expert grader and the corresponding Kappa coefficient was determined for overall grading, referable, non-referable and un-gradable disease.

Results. The inter-grader agreement between the primary graders and the expert grader bettered the audit standard of 80% in all the categories. The Kappa co-efficient ranged from moderate to substantial (0.59 to 0.7).

Conclusions. The audit confirmed the accuracy of the primary graders in the Bristol and Weston diabetic retinopathy screening programme when compared to a blinded expert grader.

THE SPECTRUM OF R3 IN PATIENTS WITH TYPE 1 DIABETES: PROBLEMS AT THE SCREENING HOSPITAL INTERFACE

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Purpose. To highlight problems encountered in the retinopathy screening program and to stimulate discussion on whether special arrangements for certain Type 1 diabetic (T1D) patients are required.

Methods. Retrospective case note review of 8 T1D patients.

Results. Patients were aged between 21-49 years and disease duration was up to 30 years. Group 1 consisted of 3 individuals whose standard screening views suggested little evidence of retinopathy, yet they presented to the hospital eye service with advanced peripheral proliferative disease and fluorescein angiography confirming severe ischaemia. Group 2 included 4 patients who opted out of medical care and screening but presented to the ophthalmic casualty with complications of R3 ie vitreous haemorrhage.

Conclusions. There appears to be a sub-group of T1D patients who develop peripheral R3 with minimal other change in the posterior pole, thus not easily detectable by standard screening procedure. There is also a group of patients who fail to attend screening and present with R3, which is difficult to treat. We should consider alternative strategies to engage these groups such as slit lamp examination of longstanding T1D patients and education of young patients who fail to understand the long-term consequences of neglecting their disease.

AUDIT ON THE DIABETIC EYE CARE SCREENING AT ST. THOMAS' HOSPITAL, LONDON

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Purpose. To determine whether referred patients are being seen within the stipulated timescales and to determine the rate of diabetic maculopathy referrals with Clinically Significant Macular Oedema (CSMO).
Methods. Prospective data collection of all patients referred from Diabetic Eye Care Screening (DECS) over a 2-month period from July to September 2008. Data was collected using proformas designed to determine time scales and reason for referral, along with final diagnosis and outcome. Workbook 4.2 from the National Screening Committee was used as a guideline for the timescales. The rate of confirmation of CSMO by OCT was also analysed.
Results. Data on 100 individuals was available for analysis; mean age 57.6yrs SD:16.9 (range: 24-89yrs). Female to male ratio was 52: 48%. 95% of referrals were for diabetic retinopathy or maculopathy. 60% of routine referrals (13 weeks), 70% of soon referrals (4 weeks) and 77% of urgent referrals (2 weeks) exceeded the recommended waiting timescales. 61% of those referred with advanced maculopathy had CSMO, confirmed by OCT.
Conclusions. More than 60% of referrals are over shooting the stipulated waiting times, but 60% of the maculopathy referred, although fulfilling the referral criteria is not CSMO. OCT confirmed CSMO in 61% of advanced maculopathy grades and we would recommend using OCT in primary grading centres.

SCREENING CLINIC NON-ATTENDANCE AND THE RISK OF SIGHT THREATENING RETINOPATHY

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Purpose. To determine if missed screening clinic appointments are a marker for sight threatening diabetic retinopathy.
Methods. Using data from the software used to run the Somerset DRSS, we have studied new patients who attend the clinic after missing one or more of their previous invitations, and have correlated this with the retinopathy level assigned at the time of attendance.
Results. Three groups have been studied: 100 new patients attending at the first invitation, 100 patients who missed their first appointment, and another 100 patients who attended after missing their first two appointments:

	no retinopathy	non-referable retinopathy	referable retinopathy
Group 1	59	37	4
Group 2	59	34	7
Group 3	51	37	12

To work out if clinic non-attendance leads to higher rates of referable retinopathy we have combined the data from 1 or >1 DNA, and looked at the proportion of referable retinopathy. This leads to a 2x2 contingency table and Fishers exact test gives a probability of 0.068. Thus there is a trend approaching significance on this data.
Conclusions. Clinic non-attendance is likely to be a risk factor for sight threatening retinopathy, and screening programs should make every effort to target this group.

DIABETIC RETINOPATHY IN A POPULATION WITH REGULAR SCREENING FOR TYPE 2 DIABETES MELLITUS AND EYE DISEASE

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Purpose. In the community of Laxå, County of Örebro, Sweden, this has been done since 1983. We evaluate diabetic retinopathy in this population.
Methods. All persons in the community of Laxå with a diagnosis of type 2 diabetes mellitus participated in the study. Diabetic retinopathy was evaluated by fundus photography and graded by an experienced ophthalmologist. The data were analysed using the SAS software release 6.12.
Results. Of the 263 diabetic patients included in the study, 172 had no retinopathy, 91 had any retinopathy. 62 patients had mild retinopathy, 20 patients had moderate retinopathy, 5 patients had severe retinopathy and 4 patients had proliferative retinopathy. 7 patients had macular oedema. The frequency of diabetic retinopathy increased from 12.5% when the duration of diabetes was 0-1 year, to 75% when the duration was more than 25 years.
Conclusions. Our study, with a screened diabetes population and high prevalence of diabetes, shows similar prevalence of diabetic retinopathy as the other Nordic studies. We have shown in an earlier study that the visual acuity lost by diabetic retinopathy is very low. The key to success in the treatment of diabetic retinopathy is finding the patients and finding the significant retinopathy.

AUDIT OF EXPEDITED REPORTS ISSUED BY DIABETIC RETINOPATHY SCREENING PROGRAM (DRSP) NORTHERN IRELAND APRIL 06 - MARCH 07

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Purpose. The aim of this audit was to assess: 1) The expedited report pathway; 2) The time scales involved in each step of the pathway; 3) Performance according to regional standards; 4) Accuracy of grading.
Methods. All expedited reports for a one-year period (1st April 2006-31st March 2007) were identified using archived reports. For each report the GP was contacted by phone and asked to provide the following information: 1) Date on which they referred the patient to the HES in response to recommendation by DRSP; 2) A copy of all written information received by the practice from the HES subsequent to the patient being referred as recommended by DRSP. The information received was analysed and in cases with discrepancy between clinical findings and screening findings the screening images were reviewed.
Results. 54 expedited reports were sent representing 0.3% of total screened and 5% of total referrals. The reporting pathway was found to have a number of steps at which delays were occurring. This made it hard to achieve locally set standards. 6.1% (2 cases) were over graded.
Conclusions. Changes need to be made to a number of steps in the pathway and are detailed in the audit. In light of the audit results the standards need to be and reassessed to establish if they are indeed realistic and achievable.

PATIENT SATISFACTION WITH A CHANGE IN THE METHOD OF SCREENING FOR DIABETIC RETINOPATHY FROM A CLINIC BASED SERVICE TO A MOBILE PHOTOGRAPHIC SERVICE

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Purpose. Assess satisfaction with both screening services and identify problem areas.
Methods. Postal satisfaction survey of all patients screened between January 1st 2007 and April 30th 2007 (n=331) who had previously attended the eye clinic for screening. Study setting rural North West Ireland. Service dimensions investigated were interpersonal, technical, facilities, accessibility and information aspects. Satisfaction items rated using 11-point scale from 0 to 10 where 10 indicated very satisfied. Differences in mean statistical levels between patient subgroups examined using t-tests.
Results. 52.5% response rate. Mean overall satisfaction score mobile unit 9.11 versus 9.21 eye clinic. Lowest satisfaction scores for clinic waiting time 8.28 versus 9.43 mobile unit. Lowest satisfaction scores mobile service privacy 8.3 and 8.81 waiting area. No statistically significant differences between overall satisfaction levels based on gender, age, use of dilating drops and proximity to screening services. No statistically significant difference overall satisfaction levels mobile unit screen negative patients 8.95 and screen positive 8.68 (Independent t-test, f =.77, sig. (2-tailed) =.494, t=.686).
Conclusions. Acceptable screening method in an Irish context with modification of mobile unit facilities required for future services.

ASTEROID HYALOSIS AND DIABETIC RETINOPATHY SCREENING

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Purpose. The aim of the study was to assess the impact of asteroid hyalosis (AH) on diabetic retinopathy screening programmes.
Methods. All AH cases were identified within the Walsall diabetic population over 18 months (a total of 9590 patient screens).
Results. 47 (0.5%) patients were identified with AH - 29 male, mean age 73.8 yrs (SD 11.3, range 46-91) and 18 female mean age 72.7 (SD 9.6 range 53-95). The ethnic groups were of White Caucasian (N=30), Asian (12) and Black Caribbean(5)origin. Mean HbA1c was 7.4% and the majority were being treated for hypertension and dyslipidaemia. e-GFR was <50mls/min in 10 patients. AH was uniocular in 43, and bilateral only in four patients. Visual acuity was 6/12 or better in 40 affected eyes. Visual acuity 6/18 or worse was due to cataracts in five eyes, corneal scarring, ARMD or amblyopia in one eye, and unexplained in two eyes. Grading was achieved in 10 patients but was not possible in 37 patients (79%).
Conclusions. This survey confirms that AH occurs in an elderly population, in different racial groups, is usually unilateral and is more common in men. Control of diabetes does not appear to be a risk factor but renal failure may possibly contribute. Ungradable images due to AH required screening by slit lamp assessment and need long-term follow-up in ophthalmology in 0.4% of the screened diabetic population.

SYNERGISTIC DIABETIC RETINOPATHY SCREENING AND OPTOMETRIC SERVICE PROVISION IN AN OPTOMETRY CLINIC SETTING

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PURPOSE. To evaluate the effectiveness of a combined optometric and ophthalmological service to patients with diabetes.
METHODS. All patients underwent a full, dilated ophthalmic examination by an ophthalmologist. A disc-centred and a macula-centred fundus image was taken OU. Images were graded and reported to the referring hospital. Patients were offered a refractive eye examination undertaken by supervised optometry students. A patient satisfaction questionnaire was also undertaken. This poster represents a retrospective analysis of 115 patients.
RESULTS. The salient findings include: 1) Refractive and medical interventions (a) 54 patients benefited from update of their refractive correction, (b) one patient was registered legally blind and another referred for low visual aid assessment, (c) medical referrals included two patients for focal laser and a further two patients for cataract surgery, (d) one patient was identified as glaucoma suspect. 2) Only 8.3% of individuals surveyed, cited control of blood glucose levels as being the most important factor in the prevention of diabetic retinopathy. 3) Patient satisfaction with the combination of optometric eye examination and diabetic screening is high. CONCLUSIONS. The above findings indicate the need to improve patient education regarding the importance of blood sugar control in the prevention or stabilisation of diabetic retinopathy. The provision of combined ophthalmological and optometric services appears to enhance patient management in terms of visual outcome and service delivery.

SCREENING METHOD IN DIABETIC RETINOPATHY

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PURPOSE. The aim was to determine sensibility and specificity of diabetic retinopathy assessments by diabetologists using nonmydriatic fundus photography (NMDFP). The study also compared clinical fundus examination with NMDFP.
METHODS. 131 patients with diabetes mellitus underwent NMDFP (Canon CR6-45NM) and were classified in three groups (normal, suspect, abnormal) by both a diabetologist and an ophthalmologist. Diagnostic results were compared (ophthalmological assessments were taken as gold standard). 49 of these patients also underwent clinical fundus examination with direct ophthalmoscopy in mydriasis by a second masked ophthalmologist (considered as gold standard), and these data were then compared to NMDFP results. RESULTS. Of the 131 digital images, 88, 30 and 13 were graded by the diabetologist as normal, suspect and abnormal respectively; for the ophthalmologist, the results were 115, 15 and 1. Sensibility and specificity were 87.5% and 75.0%, respectively. The agreement between specialists was moderate (kappa=0.38). Of the 49 eyes, 46 and 3 were respectively graded as normal and abnormal based on clinical results; and 43 and 6 for the NMDFP. The agreement between methods (k=0.64) and specificity (94%) were good. CONCLUSIONS. Digital non mydriatic fundus images are noninvasive and easy, and offer a good sensibility and specificity. The concordance between diabetologist and ophthalmologist, and between clinical ophthalmoscopy and digital photography were acceptable, thus showing the potential use of digital fundus photography in the screening of diabetic retinopathy.

PATIENT SATISFACTION WITH DIABETIC RETINOPATHY NSC SCREENING OUTCOME REPORTS

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PURPOSE. To assess satisfaction and whether the wording required modification.
METHODS. A postal questionnaire was sent prospectively to 154 consecutive patients. The standardised and validated questionnaire assessed several criteria on the reports, including patient satisfaction with content, presentation, and on the usefulness of the information contained within. There are 6 standard outcome letters, representing each retinopathy subgroup.
RESULTS. We distributed questionnaires to: 40 normal, 40 background, 2 preproliferative, 60 proliferative, 4 maculopathy, 8 technical screening failures. 34 patients responded: 9 normal, 9 background, 1 preproliferative, 2 proliferative, 7 maculopathy, and 6 could not identify their subgroup. 85% found the reports helpful/useful. 76% felt they were easy to understand and 82% felt they were well presented and easy to read. 15% felt they were not detailed enough and 18% felt they were unclear and did not answer questions on the subject. 68% felt well-informed and 70% were reassured, however 15% felt they were frightened and 30% were anxious by the reports. 55% of patients felt they would like the report to

be explained to them by their GP or hospital.
Conclusions. Overall, patients seemed to be satisfied with the outcome reports in their current format.

ACUTE ANGLE CLOSURE GLAUCOMA FOLLOWING MYDRIASIS FOR DIABETIC RETINOPATHY SCREENING

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Purpose. To assess the frequency of acute angle closure glaucoma (AACG) following mydriasis for diabetic retinal screening(DRS) (with tropicamide 1% only) in Dorset and present the details of these cases.
Methods. The notes of all AACG cases presenting between 1st April 2007 to 31st March 2008, to the two eye units serving Dorset, were scrutinised to ascertain how many had been caused by mydriasis for DRS. The details of these patients were collected.
Results. Of the 27 cases in this time period there was 1 case in which this had occurred. There was also another case occurring outside this time period and one case in which angle closure was present before dilation was performed. During this time 22093 people were screened for diabetic retinopathy in the community. This would estimate the rate at 0.0045%. We present our cases.
Conclusions. AACG after mydriasis for diabetic retinal screening is rare but may be occurring at a higher rate than previously reported. In line with current national screening guidelines we recommend that patients are warned of this prior to, and after dilation with written information advising them how to seek immediate attention if this occurs.

DIABETIC RETINOPATHY SCREENING PROGRAMME NORTHERN IRELAND - THEN AND NOW

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Purpose. The programme represents a quality assured regional service for a population of 1.84 million, with the estimated number of people with diabetes mellitus* being 60822. The programme aims to offer comprehensive, easily accessible screening to diabetic people of 12 years and older.
Methods. The programme provides digital retinal imaging for the 4 Northern Ireland Commissioning Bodies (Northern, Southern, Eastern and Western Area Boards). 3 of these are served by 8 mobile units which visit primary care facilities. Image capture for the 4th body (Western Area Board -population 312,000) is at 6 static sites.
Results. The programme has changed and expanded over the last decade and this is partly demonstrated by the following figures: 2006/07, 27,258 patients invited for screening, uptake 70%; 2007/08, 34,647 patients invited for screening, uptake 64%; 2008/09, estimated 42,000 patients invited for screening, uptake estimated 70% (final figures available 31.03.09).
Conclusions. This quality assured programme has evolved greatly since its conception. Above all the aim of this maturing team remains the detection of sight threatening diabetic retinopathy.

USE OF SPECTRAL-DOMAIN OCT IMAGING TO FACILITATE MACULOPATHY REFERRALS FROM SCREENING PROGRAMMES

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Purpose. To evaluate a new patient care pathway using a spectral-domain optical coherence tomography (SDOCT) clinic to assess patients with referable maculopathy (M1) and low levels of retinopathy (R0 or R1).
Methods. Prospective audit of patients referred from screening with M1/R0-R1 maximal retinopathy in either eye attending an SDOCT screening clinic. We used a previous retrospective audit of M1 referrals to inform this study design. The images were graded by the ophthalmologist as SDOCT positive (macular oedema present) or SDOCT negative. SDOCT positive patients were referred to the medical retina clinic. SDOCT negative patients were reviewed in the SDOCT screening clinic in 6 months and images were again graded.
Results. Images from 90 patients were used in the analysis. The mean interval between screening and OCT imaging was 6.8 weeks. There were 31 OCT positive patients (38%) and an additional patient (1%) referred due to ungradable OCT images. Six (7%) patients were referred for other macular disease. There were 52 OCT negative patients (58%); 49 (54%) were not referred to clinic but rescreened in the OCT clinic with 3 (3%) referred due to retinopathy.
Conclusions. SDOCT imaging is a useful adjunct to diabetic retinopathy screening in a well-defined screening population subset following a well-defined protocol with careful supervision by an ophthalmic team and warrants further study.

3D OCT IMAGING AND RETINAL PHOTOGRAPHY AS A FOLLOW-UP TOOL FOR DIABETIC MACULOPATHY AND STABLE RETINOPATHY. THIS IS CAUSING CAPACITY ISSUES IN THE NHS

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Purpose. To assess the role of 3D OCT imaging combined with retinal photographs alone in evaluating patients with maculopathy and mild to moderate non-proliferative diabetic retinopathy (NPDR).
Methods. People attending medical retina clinics for diabetic retinopathy were assessed by an ophthalmologist and also had Topcon 3D OCT assessment combined with 2 retinal photographs of each eye. Patients undergoing a course of laser treatment, or with previously known severe/ very severe NPDR were excluded from analysis. The images alone were assessed by another ophthalmologist, who was masked to the outcome of the clinic assessment.
Results. 53 patients were included. Following clinical consultation 7 (13%) were listed for macular laser treatment, and 23 (43%) were booked for further follow-up within 6 months. When the OCT and retinal images alone were assessed, it was determined that 23 (43%) patients would need a recall for further clinical review or treatment. This included all patients listed for laser treatment on the clinic visit.
Conclusions. The use of 3D OCT with retinal photographs alone for patients with early maculopathy and mild/ moderate NPDR appears be a suitable technique to allow certain patients to be followed-up by imaging alone, which could improve capacity issues within the hospital eye service.

EFFECT OF INTRAVITREAL TRIAMCINOLONE INJECTION ON DIABETIC MACULAR OEDEMA: ANATOMO-CLINICAL CORRELATIONS

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Purpose. The aim of the study is to assess the effect of a triamcinolone intravitreal injection on functional and anatomical retinal findings, and to correlate these findings between them, in patients with refractory diabetic macular oedema.
Methods. Seven patients (8 eyes) with cystoid diffuse refractory diabetic macular oedema received a 4 mg triamcinolone intravitreal injection. All the patients underwent, before and one month after injection, ETDRS visual acuity, contrast sensitivity (CS) (Pelli-Robson method), Stratus and Cirrus Optical Coherence Tomography (OCT) examinations.
Results. Before injection, the ETDRS and CS scores were weakly correlated, and the ETDRS score was better correlated with the OCT findings than the CS score. After injection, the ETDRS and CS scores were better correlated, and the CS score was better correlated with the OCT findings than the ETDRS score. After injection, the ETDRS score and the number of eyes with a visible photoreceptor cell line on OCT were non significantly increased, whereas the CS and the macular thickness and volume were significantly improved.
Conclusions. In refractory diabetic macular oedema, the anatomical and functional findings seem to be weakly correlated, before and after injection. The CS may better assess the functional improvement after injection than the visual acuity. The triamcinolone intravitreal injection may lead to a recovery of the photoreceptor cell line on OCT.

NON-UNIFORM SPATIAL DISTRIBUTION OF MACULAR LESIONS IN TYPE 2 DIABETES

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Purpose. To record and report the location and spatial distribution of retinal lesions in relation to the fovea in patients with type 2 diabetes.
Methods. Location, type and area of retinal lesions from 1338 digitised macular–centred images in 747 people were quantified using an on-screen recording tool. Location data of microaneurysms (MA), blot haemorrhages (BH), hard exudates (HE) and IRMA from all images (right and left eyes superimposed) were summated to produce distribution data and density maps.
Results. Temporal, superior, nasal and inferior quadrants (centred on the fovea) contained 41%, 22%, 19% and 18% respectively of all MA, 41%, 23%, 15% and 21% of all BH, 49%, 25%, 12% and 14% of all HE and 64%, 15%, 5% and 16% of all IRMA. HE distribution showed an area of high density superior-temporal to the fovea which was not found in the other lesions analysed.
Conclusions. The distribution of macular field lesions is not uniform. For MA, BH and HE the greatest density is in the region temporal to the fovea, particularly along the horizontal watershed. This unequal spatial distribution may provide new data on diabetic macular physiology and future risk of reduced visual acuity.

STRUCTURAL AND FUNCTIONAL CHANGES OF THE FOVEA IN PATIENTS WITH DIABETES MELLITUS AND NO OR MINIMAL DIABETIC RETINOPATHY

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Purpose. To evaluate the possible correlation between macular retinal thickness (RT) measured with Fourier-domain optical coherence tomography (FD-OCT) and the function of the fovea measured with the Rarebit Fovea Test (RFT) in diabetic patients with no or minimal diabetic retinopathy (DR).
Methods. Fifty patients, recruited from the outpatient clinic of the department of Internal Medicine at the Academic Medical Centre (University Hospital, Amsterdam, the Netherlands), underwent ophthalmic examination, stereoscopic fundus photographs, FD-OCT and RFT. Control subjects (n=50) were age and gender matched with patients.
Results. The mean RT in the pericentral area of the macula was thinner and the RFT results decreased in diabetic patients compared to controls. The mean RT and foveal function showed a significant correlation and were both related with the duration of diabetes mellitus.
Conclusions. The thinning of the pericentral retina in diabetic patients is associated with functional loss of the fovea and supports the concept that early DR includes a neuro-degenerative component.

IMPROVING SCREENING FOR DIABETIC RETINOPATHY IN PREGNANCY: NEW NICE GUIDELINES – AIMING TO MEET THE STANDARDS

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Purpose. To look at the current screening of diabetic retinopathy in pregnant patients at the Royal Berkshire Hospital, apply improvements to the system of referral and follow- up and review the impact of these changes.
Methods. Notes review of diabetic pregnant patients in Berkshire (August 2008-January 2009).
Results. The study showed only 26% of patients were seen in accordance with recent NICE guidance prior to instigating any improvements. Several weaknesses were identified: referral from obstetrics to ophthalmology, patients who do not attend appointments being "lost", and inadequate booking procedures to make timely appointments. The following were instituted: Information leaflets given to all pregnant diabetics by obstetricians, emphasising need for eye examination and contact numbers to improve compliance; electronic tracking of patients' progress; fail safe officer to contact if appointment not received, to track progress and re-schedule appointments; block booking of follow-up appointments at first visit, ensuring timely follow-up; improved feedback to GP and community screening service. Following implementation, preliminary results show improvements in numbers of patients referred from obstetrics and tracking of patients. Patient compliance regarding appointment attendance still remains variable.
Conclusions. Simple measures including better communication with obstetricians, GPs and the community screening service; tracking patients and a fail safe officer may help achieve standards recommended by NICE for care of diabetic pregnant patients. Poor attendance of appointments remains a problem and requires further attention.

HYPERBARIC OXYGEN THERAPY DOES NOT SEEM TO AGGRAVATE DIABETIC EYE DISEASE

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Purpose. To evaluate the effects of HBOT on diabetic eye disease during one year follow-up.
Methods. A prospective randomized double-blinded study was performed. Patients were randomized to either 40 sessions of HBOT (100% oxygen at 2.5 bar for 90 minutes) or 40 sessions of hyperbaric air treatment (2.5 bar for 90 minutes). Visual acuity (VA), levels of diabetic retinopathy (DRP, modified Wisconsin method) and presence of clinical significant macular edema (CSME) were evaluated before, 2, 6, and 12 months after treatment. All evaluations were performed by an experienced ophthalmologist.
Results. 63 diabetic patients (19 type1)were included (32 HBOT, 31 air). HbA1c 6.9%± 1.6 vs 7.0% ± 1.4; NS. Diabetes duration 23±14 vs 22± 15NS. No statistically significant difference or trends towards differences in VA, level of retinopathy or frequency of CSME were seen between the groups during 1 year follow-up.
Conclusions. In this small placebo controlled double-blinded study HBOT did not aggravate diabetic eye disease.

A CROSS-SECTIONAL SURVEY OF DEPRESSION, ANXIETY AND COGNITIVE FUNCTION IN OUTPATIENTS WITH TYPE 2 DIABETES

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Purpose. To evaluate prevalence and severity of depression and anxiety in a population of T2DM outpatients and their possible correlation with cognitive function and clinical variables.
Methods. Cross-sectional study. Depression and anxiety were assessed by the relevant Zung-questionnaires and cognitive status by the Minimal-Mental-State test. In total, 498 questionnaires were administered to T2DM patients aged 40-80, 249 Non Insulin-Treated (NIT) and 249 Insulin-Treated (IT).
Results. The overall prevalence of depression was 16.5%, compared with a reported 3-9% in the general population. NIT differed from IT patients for age (66.20±8.05 vs 68.96±8.05; $p>0.01$), known duration of diabetes (13.77±7.11 vs 20.27±8.03; $p<0.01$), fasting glycaemia (150.97±39.26 vs 173.53±67.42; $p<0.01$) and HbA1c (7.85±1.23 vs 8.46±1.48; $p<0.01$). More IT patients practiced self-monitoring ($p<0.01$) and did more daily measurements ($p<0.01$). However, IT and NIT patients did not differ for depression, anxiety or cognitive impairment. Although foot ulcers, retinopathy and microalbuminuria were more frequent in IT patients ($p<0.01$, all), these did not correlate with depression or anxiety. Anxiety ($r=0.216$; $p<0.001$) and depression ($r=0.129$; $p=0.0045$) correlated, in IT patients, with BMI.
Conclusions. These data confirm an increased prevalence of depression and anxiety in T2DM. However, the lack of correlation with disease duration, metabolic control or microvascular complications suggest that depression may predate diabetes rather than appear/worsen during its progression and with the onset of complications.

IDENTIFICATION OF RISK FACTORS FOR THE DEVELOPMENT OF DIABETIC RETINOPATHY REQUIRING TREATMENT

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Purpose. To identify associated variables to reaching a treatment endpoint and devise a model to improve screening based on these.
Methods. Multiple logistic regression weighted according to principles of IPTW was used to make correlations between risk factors and treatment.
Results. Men with type 1 diabetes reached a treatment end point after a shorter disease duration than women, whereas no such difference was found among patients with type 2 diabetes. The risk of reaching a treatment end point was in both diabetes types independently affected by retinopathy grade and HbA1c. Furthermore, in type 1 diabetic patients the risk of reaching a treatment end point was independently affected by disease duration and by a recommended control interval of less than 3 months, in spite of correction for retinopathy grade and other studied confounders, whereas in type 2 diabetes this risk was affected by increasing age of diagnosis of the disease.
Conclusions. Only a subset of known risk factors for development and progression of diabetic retinopathy should be used to construct a decision model for optimizing screening intervals for diabetic retinopathy.

IS IT NECESSARY TO USE TOPICAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN ADDITION TO TOPICAL STEROIDS POST-CATARACT SURGERY ROUTINELY IN ALL DIABETIC PATIENTS?

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Purpose. To study the progression of retinal changes following cataract surgery in diabetic patients with normal fundus or mild NPDR treated post-operatively with topical steroids alone compared to topical steroids and topical NSAIDS.
Methods. Retrospective case-notes review of patients with diabetes with either mild NPDR (without maculopathy) or no retinopathy, who underwent uneventful cataract surgery (phacoemulsification) in our medical retina unit from May 2005 to July 2008. Patients with maculopathy or other fundus pathology were excluded. Patients were categorised in to: Group 1: Patients on topical steroids and topical NSAIDS. Group 2: Patients on topical steroids only. We collected data on patient demographics, best corrected visual acuity preoperatively, 3 and 6 months post-operatively, grade of diabetic retinopathy and maculopathy pre- and 3-6 months post-operatively.
Results. 90 eyes in group 1 and 94 eyes in group 2 fulfilled inclusion criteria. Male: female ratio was 1.7:1 in group 1 and 1.2:1 in group 2. Age range was 49-92 years in group 1 and 48-89 years in group 2. In group 1, 31% had NPDR and 69% had no retinopathy. In group 2, 43% had NPDR and 57% had no retinopathy. Progression of diabetic retinopathy was noted in 2/90 eyes (2.2%) in group 1 and 2/94 eyes (2.1%) in group 2. In group 1, 3/90 eyes (3.3%) and group 2, 3/94 (3.2%) developed clinically significant macular oedema within 6 months of cataract surgery.
Conclusions. In this study no difference was found in the incidence of progression of diabetic retinopathy and maculopathy in diabetic patients with mild NPDR or no diabetic retinopathy post cataract surgery in patients treated with top-

ical steroids only compared to those treated with topical steroids and topical NSAIDs. Therefore addition of a topical NSAID may not be beneficial in this group of patients.

CHRONIC FOOT ULCERS ARE ASSOCIATED WITH DIABETES RELATED OPHTHALMOPATHY

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Purpose. The aim of the present study was to evaluate if patients with chronic foot ulcers had more severe diabetic retinopathy than patients without a history of chronic foot ulcers.
Methods. Visual acuity (VA), retinopathy level according to the modified Wisconsin scale, frequency of clinical significant macular edema (CSME) and given panretinal scatter treatment were evaluated in 63 patients with foot ulcers of a duration of more than 3 months (UG). The control group consisted of randomly selected patients from the diabetes register of the Eye Department (CG).The patients were matched for type of diabetes, age and diabetes duration.
Results. Both groups consisted of 19 patients with Type 1 and 44 patients with Type 2 diabetes. Age 64.6±12.7 years (UG) vs 63.5±63.5 years (CG), NS. Diabetes duration 23± 14 years. Level of retinopathy mean 41 vs 21/31, $p<0.001$. VA 46 vs 49 ETDRS letters, $p<0.05$. CSME 18% vs 1.5%, $p<0.05$. Scatter treatment 36% vs 14%, $p<0.001$.
Conclusions. The levels of retinopathy, the frequencies of CSME and scatter treatment were higher in the patient group with chronic foot ulcers compared to the group without.

CORNEAL DIABETIC NEUROPATHY: A MODEL FOR DIABETIC NEUROPATHY

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Purpose. To investigate corneal subbasal nerve plexus changes in CDN using corneal confocal microscopy.
Methods. Thirty-six consecutive diabetic patients affected in both eyes by CDN (subbasal plexus nerve changes) were investigated and followed using corneal confocal microscopy (Confoscan4, Nidek, Japan). A new validated technique for subasal nerve plexus detection and examination was applied. Corneal confocal microscopy parameters for nerve changes were: number and density of nerve fibers, nerve tortuosity and branching, number of nerve beadings. Two masked examiners evaluated and quantified corneal confocal microscopy images.
Results. Corneal confocal microscopy allowed in all 72 eyes a quantitative analysis of subbasal nerve plexus. Intra and inter-examiner agreement for confocal microscopy images were almost perfect ($k= 0.95$ and 0.92, respectively). Significant increase of nerve beadings ($p <0.005$) and reduction in nerve tortuosity ($p<0.004$) were the distinctive parameters of nerve regeneration. Increase of nerves density and fibers was a late phaenomenon.
Conclusions. These results show that corneal confocal microscopy is the key diagnostic technique in evaluating and monitoring CDN. Quantification of corneal subbasal nerve plexus parameters allows a correct, reproducible and objective, in vivo, non invasive approach to CDN, allowing to characterize peripheral diabetic neuropathy, a potentially highly disabling complication of diabetes.

IMPROVING MANAGEMENT OF PATIENTS WITH PROLIFERATIVE DIABETIC RETINOPATHY (R3) AUDIT, CHANGE OF PRACTICE, REAUDIT

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Purpose. To determine if the management changes of patients with R3 were successful in improving standards of care.
Methods. Of 16,553 screened in one year, 56 were graded as R3. The pathway from grading to hospital clinic appointment was assessed by retrospective analysis of case notes. The outcomes were compared to NSC standards. The process was reaudited for 6 month period to assess the impact of changes.
Results. The initial audit results showed the national targets were not met. After analysis of the apparent reasons for failure, changes were made to the referral pathway process, tracking procedures were introduced and fail-safe mechanisms developed. These are described. This achieved an improvement in the management of these patients.
Conclusions. Implementation of new processes achieved a significant improvement in the standard of care for those diabetic patients referred to the local district general hospital with R3 disease. The reaudit demonstrates useful techniques that could be adopted by other units without advanced IT systems to improve standards of care for those referred with high risk sight threatening diabetic retinopathy.

PROLIFERATIVE DIABETIC RETINOPATHY AND COMPLICATIONS DUE TO COEXISTING AUTOIMMUNE DISEASES

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Purpose. Description of aggressive diabetic retinopathy in 2 patients with autoimmune multiglandular disease.
Methods. Clinical case presentation of 2 young female siblings suffering from autoimmune multiglandular insufficiency, complicated with severe sight threatening diabetic retinopathy in their early twenties.
Results. Both patients were diagnosed with Type 1 diabetes and coeliac disease in early childhood. The elder sister further suffers from hypertension, hypothyroidism, SLE with vasculitis complicated with DVT and pulmonary thrombosis, partial epilepsy and osteopenia. The younger sister suffers from a not yet diagnosed rheumatic disease, suspicious for SLE, and has been diagnosed with nephrolithiasis and pyelonephritis. Both patients have developed aggressive proliferative retinopathy. Because of diet restrictions and drugs such as prednisolone and disease-modifying antirheumatic drugs used to treat their coexisting diseases, good glucose control has been difficult to achieve, and anticoagulation therapy has further increased the risk of vitreous haemorrhage.
Conclusions. Interdisciplinary collaboration, knowledge of related autoimmune disorders, with special attention on development of potential life threatening diseases such as Addison's disease, is necessary to enhance quality of life, optimize treatment and minimize complications in patients with multiglandular diseases.

ASYMMETRIC CHANGES IN MILD PRE-PROLIFERATIVE DIABETIC RETINOPATHY IN A PATIENT WITH UNILATERAL INTERNAL CAROTID ARTERY OCCLUSION: CASE REPORT

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Purpose. Carotid artery occlusions (CAO) can produce a similar type of ischaemic retinal symptoms as caused by other diseases or disorders. The purpose of this study is to analyse the course of diabetic retinopathy with the emphasis on the importance of early detection and diagnosis of CAO.
Methods. 56 year old man with a 28-year history of type 2 diabetes presented for routine examination with his ophthalmologist. His visual acuity was 0.5 and intraocular pressure 12 mmHg in both eyes. He underwent bilateral fundal examination with photography and fluorescein angiography.
Results. No endarterectomy was performed. Doppler ultrasound of carotid arteries revealed left internal carotid artery complete occlusion and Leriche's syndrome and diabetic retinopathic changes were more advanced in the left eye. At 3 months ophthalmologic follow-up showed deterioration of vision to CF caused by hyphaema.
Conclusions. Early detection of CAO and surgical intervention, if indicated, is extremely important for improved retinal outcomes. Collaboration among ophthalmologists, diabetologists and other specialties is essential for improved multispecialty outcomes in the specialty care setting.

EFFECTIVE GLYCAEMIA AND ARTERIAL BLOOD PRESSURE MANAGEMENT IMPROVES THE OUTCOME OF LASER COAGULATION IN HYPERTENSIVE PATIENTS WITH DIABETES MELLITUS

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Purpose. Poorly controlled diabetes mellitus (DM) and high arterial blood pressure (ABP) are major risk factors for retinopathy development. Fifteen years from diagnosis, ~50% of people with Type 1 and 80% with Type 2 DM develop proliferative retinopathy (PDR). Laser coagulation (LC) is the most effective therapeutic approach to PDR and macular oedema (MO). The aim of the present work was to show that LC performed when glycaemia and ABP control is good, prevents PDR progression and decreases the rate of relapse.
Methods. Patients with PDR (n=52, 88%) and MO (n=7, 12%) were divided into 2 groups: Gr. 1 (n=37), systolic BP (SBP) 160±15 mmHg and microalbuminuria (MA) 80±20 mg/L; Group 2 (n=22), SBP 162±20 mmHg and MA 85±23 mg/L. At entry mean fasting (FBG) and postprandial (PBG) blood glucose and HbA1c levels in both groups were FBG 140±15 mg/dL; PBG 230±30 mg/dL; HbA1c 12.4±2.5%. Glycaemia and ABP control was normalised in both groups before LC was performed: Gr. 1 intensive insulin therapy and aggressive antihypertensive treatment; Gr. 2 oral hypoglycemic agents and less tight ABP control. LC comprised ~2500 panretinal burns for PDR and standard grid for MO.
Results. At 3 months, glycaemia and ABP indices had improved: FBG 105±10 mg/dL; PBG 160±20 mg/dL; HbA1c 7.6±1.5%. In Gr. 1, SBP and MA were normalized (130±10 mmHg and 25±9 mg/L, respectively); in Gr. 2, SBP and MA 142±15 mmHg and 38±12 mg/L, respectively. At 3 months, LC was successful in 49/52 PDR patients; in 3 (5.8%) cases from Gr. 2, where glycemia and ABP control was less strict, relapse occurred. Hard exudates cleared and vision improved in MO eyes.
Conclusions. In this study population strict glycaemia and ABP control resulted in better outcomes in patients with PDR and MO.