Reassuringly, 72% knew that FH should be considered in adults with a total cholesterol >7.5mmol/l, but just 56% were aware of or had used the Simon Broome criteria. Further, while 61% were aware of the NICE guidelines, just 12% had actually used them.
Disappointingly, while 32% had detected FH in a first-degree relative of a patient already diagnosed with FH, 31% were not aware of the indications for cascade testing, Similar numbers believed the diagnosis requires genetic testing. This reflects the finding that only 50% knew the prevalence of FH in the United Kingdom and 54% the pattern of inheritance. 78% underestimated the relative risk of premature death associated with FH.
Worryingly, just 8% thought their region managed FH well. 69% believed that better access to specialist lipid clinics would improve care and 74% felt more education would improve the identification and management of FH. These recommendations are in keeping with the results of this survey. We are investigating the effect of targeted education locally.

LONGITUDINAL STUDY OF THE IMPACT OF LIPID LOWERING THERAPY ON CAROTID ATHEROSCLEROSIS

M. Seed [1], D. Bond [2], M. Griffin [2], A. Nicolaides [1,2].

[1] *Imperial College NHS Trust, London, UK;* [2] *Vascular U/S Diagnostic Centre, London, UK*

NICE guidelines for primary prevention of CVD include reduction of LDL-C to 2 mmol/l in high risk patients and by 50% in patients with FH. We wished to see whether such levels might be achieved in a lipid clinic setting, and if so what effect this had on carotid plaque thickness and type.

Subjects: 31patients, 10 with definite FH (mean age 42), the remainder with mixed hyperlipidaemia (MHL), mean age 54, were treated, and followed up with serial carotid ultrasound examinations over a 2-9 year period. No FH patients were hypertensive or diabetic. 10 with MHL had hypertension and 3 type 2 diabetes; 6 were ex-smokers.

Methods: B mode ultrasonic assessments of plaque thickness and type were performed in all patients initially and at follow-up (mean 4 years (all); mean 6 years, n=17). Measurements were taken by a single "blinded" operator.

Results	FH (n=10)		MHL (n=21)	
	pre-Rx	Rx	pre-Rx	Rx
TC mmol/l	10.4	5.3	7.4	4.0
TG mmol/l	1.5	1.1	3.6	1.9
HDL mmol/l	1.3	1.4	1.2	1.2
LDL-C mmol/l	8.4	3.4(-60%)	4.9	2.1(-57%)
Lp(a)* mg/l	680(171-1818)	200(37-781)		

*median and range Lipid lowering therapy: Rosuvastatin 20-40mg +/- Ezetimibe 10mg.

In both groups there was a modest increase in plaque thickness (.013 mm/yr in FH, .032 mm/yr in MHL). In 3 subjects, 2 FH and 1 MHL, no increase in plaque thickness was observed. In all subjects plaque echogenicity was increased, consistent with increased fibrosis.
Discussion: In this study progression of atherosclerosis was not prevented by reduction in LDL-C to the levels recommended by present guidelines. In particular, there continued to be progression in patients with FH despite a mean reduction of 60% in LDL-C. This is in contrast to the findings of the ASAP study of patients with FH (mean age 48, baseline LDL-C 8mmol/l), in whom a reduction in LDL-C of 50.5% was associated with a reduction in intima-medial thickness of 0.03mm over 2 years. The findings of ASAP were paramount in the FH treatment recommendations made by NICE on target reductions in LDL-C in 2008.
In keeping with the results of previous coronary angiographic studies, we found a greater effect of lipid lowering therapy on plaque thickness in the FH than the MHL group,but the 50% reduction in LDL-C recommended for FH patients may not be sufficient to prevent progression of atherosclerosis.

MANAGEMENT OF FAMILIAL HYPERCHOLESTEROLAEMIA IN LIPID CLINICS – ARE WE TREATING TO TARGET?

Rahul Yadav [1], Jonathan Schofield [2], Ruth Eatough [2], Omer Pervaiz [1], Hannah Bird [1], Shashithej Koppa Narayana [1], Michael France [2,3], See Kwok [2], Handrean Soran [1,2].

[1] *University Department of Medicine, Central Manchester University Hospitals, Manchester, UK;* [2] *Cardiovascular Trials Unit, Central Manchester University Hospitals, Manchester, UK;* [3] *Department of Clinical Biochemistry, Central Manchester University Hospitals, Manchester, UK*

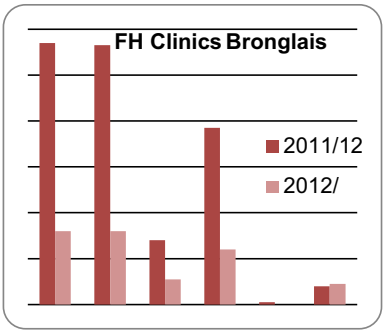
NICE guidance for the Management of familial hypercholesterolaemia (FH) recommends lipid-modifying drug therapy to achieve a reduction in low density lipoprotein cholesterol (LDL-C) of greater than 50% from baseline.

Over a thousand patients with FH are managed in our lipid clinic. This audit aimed to ensure that these patients were being treated according to NICE guidelines.
The notes of 111 consecutive adult patients with a diagnosis of FH (73% definite, 27% possible - Simon Broome criteria) who had attended the lipid clinic at least twice before (average duration of treatment 11.7 years) were reviewed.
Mean LDL-C was 6.6mmol/l at baseline, and 3.5mmol/l at follow-up, with a median reduction of 47%. Just 39% of patients achieved a 50% reduction in their LDL-C cholesterol.
NICE guidance states that healthcare professionals should consider prescribing Ezetimibe when LDL-C concentration is not appropriately controlled after statin dose titration. Ezetimibe was only prescribed for 17% of patients.
More recently, the European Atherosclerosis Society (EAS) suggested an LDL-C treatment target of <2.5mmol/l. Only 23% of our patients achieved this goal.
35% had established coronary heart disease. These high-risk patients achieved a median reduction in LDL-C of 53%, although the recommended 50% reduction in LDL-C was only achieved in 49%. Just 10% reached the EAS treatment target of <1.8mmol/l for very high-risk subjects with cardiovascular disease.
This audit suggests that many FH patients seen in specialist lipid clinics are not achieving recommended reductions in LDL-C. It is important that we consider prescribing high-intensity statins (at maximum licensed or tolerated doses), Ezetimibe, bile acid sequestrants, nicotinic acid, fibrates, and new lipid-modifying drugs when they become available for these high-risk patients to reach these targets. These results also demonstrate how difficult treating to targets can be if currently available lipid-modifying medications are not tolerated.

INITIATION OF A NURSE LED FH CLINIC FOR THE IDENTIFICATION OF INDIVIDUALS WITH FAMILIAL HYPERCHOLESTEROLAEMIA (FH) IN A RURAL SETTING

Townsend D, Gingell R, Edwards R, Datta D, Edmunds L, Haralambos K are all part of the Welsh FH Project Team. Lewis D is the Cardiac Rehabilitation Team Leader, Bronglais, McKeogh D is the Consultant Cardiologist at Bronglais, Poyser, K is Biochemist, Bronglais. Dr EJ Williams was the original clinical advisor to the FH Project. Haboubi N, is Consultant Chemical Pathologist, Hywel Dda Health Board.

Following the implementation of an All Wales FH Project in September 2010, one of the priorities was the identification of individuals who potentially had this condition in rural areas that had no lipid clinic provision.
A nurse-led FH clinic was established at Bronglais Hospital, Aberystwyth, by enrolling the support of local clinicians, specifically the local Cardiologist, Cardiac Rehabilitation Nurses, and the Clinical Biochemist. All lipid reports of a total cholesterol greater than 7.5mmol/L were automatically



flagged with a statement asking the GP query the patients family history and refer where appropriate. The same results were also flagged for review by Cardiac Rehabilitation nurses who sent a questionnaire to each patient. Responses and GP referrals that suggested the diagnosis of FH in line with the Simon Broome Clinical Criteria were then listed for review at clinic by the Specialist Lipid nurse.
Educational events were held locally for health care professionals to raise awareness of FH and aid with the identification of those who have this condition and could be referred to the FH clinic.
Of the five families assessed and newly diagnosed with a genetic mutation for FH, this has subsequently led to 40 relatives being tested with 19 being positive and additional family members yet to test. A further 17 families were identified where, although no genetic mutation was identified, family members were advised to undergo lipid testing and many of these had lipid profiles that were in line with the Simon Broome Criteria.

Abstracts Presented as Posters

LIPOPROTEINS AND LIPOPROTEIN X MEASUREMENTS IN PRIMARY BILIARY CIRRHOSIS AND PRIMARY SCLEROSING CHOLANGITIS

K. Al-Musalhi, M. Sharma, M. Sharifi, L. Robertson, J.W. Persaud, D.P. Mikhalidis, D.R. Nair.

Department of Clinical Biochemistry, Royal Free Hampstead NHS Trust, London NW3 2QG, UK

Primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) are common causes for chronic immune-mediated cholestatic liver disease in adults. Patients with PBC or PSC often present with abnormal lipid profiles but not usually associated with lipid stigmata. The serum lipids profile in these cholestatic liver disorders shows high levels of total cholesterol (TC) and presence of unusual lipoprotein particles known as lipoprotein X (LpX), an abnormal lipoprotein that is rich in free cholesterol and phospholipids. We report 2 cases of secondary hyperlipidaemia associated with lipid stigmata in cholestatic liver disease. A 35 year old lady with established serological and histopathological diagnosis of PBC was found to have a very high TC of 55.5 mmol/L and triglycerides (TG) of 11.3 mmol/L. She had bilateral xanthelasmata and palmar xanthomata. The second case is a 34 year old man with established histopathological diagnosis of PSC who was found to have very high TC of 34.6 mmol/L but normal TG of 1.5 mmol/L with extensive eruptive xanthomata and palmar xanthomata. Apolipoprotein E (ApoE) phenotyping using isoelectric focusing and electrophoresis was carried out and reported as E2/E3 in both patients. However, the ApoE genotyping revealed Apo E3/E3 isoform. Lipoprotein X may have interfered with Apo E phenotyping by isoelectric focusing. Serum lipoprotein electrophoresis showed a diffuse band in the low density lipoprotein cholesterol region but with a unique cathodic migration which is consistent with the presence of LpX. Quantification of free cholesterol and phospholipids were carried out and Lpx levels was estimated accordingly. The results were consistent with high levels of this aberrant lipoprotein in the circulation which may interfere with lipoprotein characterisation by electrophoretic technique.

INVESTIGATION OF THE EFFECT OF TESTOSTERONE TREATMENT ON THE EXPRESSION OF CHEMOKINE RECEPTORS IN MONOCYTE/MACROPHAGE THP-1 CELL LINE

H.K. Bokhamada [1], M.N. Woodroofe [1], T.H. Jones [2], S.H. Small [1], W. Kay [1], C.F. Dalton [1].

[1] *Biomedical Research Centre, Sheffield Hallam University, UK;* [2] *Academic Unit of Diabetes and Endocrinology, University of Sheffield, UK*

Introduction: Testosterone deficiency is associated with atherosclerosis development. Macrophage cells play a key role in atherosclerosis through expression of chemokine receptors CX3CR1 and CCR2 facilitating binding to the endothelium, which expresses the corresponding ligands, fractalkine (CX3CL1) and CCL2, at the luminal surface. We investigated whether testosterone replacement treatment (TRT) inhibited the expression of fractalkine receptor (CX3CR1) and CCR2 the receptor for CCL2 in the monocyte/macrophage cell line THP-1, to determine whether this could explain the effects of TRT on atherosclerosis.

Methods: Human monocyte THP-1 cells were differentiated to macrophages and treated with TRT at 10 and 100 nM with and without the androgen receptor blocker flutamide for 24 and 96 hr. Cells were also incubated with combination cytokine treatment (TNF+INFγ) at 10 and 100 ng /ml for 24 hr before and after TRT and flutamide incubation. q-PCR and flow cytometry was used to determine the expression of CX3CR1 and CCR2.
Results: TRT at 10 and 100 nM caused a trend to decrease CX3CR1 mRNA expression whereas TRT increased CCR2 mRNA expression in macrophages, an effect that was abrogated by 100 nM flutamide. 24hr TNF+INFγ reduced expression of CCR2 ($p=0.03$, $p=0.01$ at 10 and 100 ng/ml) and CX3CR1. 24hr TNF+INFγ combined with TRT induced a non-significant increase in CCR2 expression, an effect that was reversed with flutamide, CX3CR1 expression decreased with TRT, an effect that was significantly abrogated by flutamide. Flow cytometry results indicate that THP-1 cells express CCR2 and CX3CR1.
Conclusion: Our results show that TRT influences CX3CR1and CCR2 expression. CCR2 mRNA was reduced by cytokine stimulation. TRT influenced the expression of both receptors following cytokine stimulation. The mechanism by which TRT could improve atherosclerosis condition needs to be further investigated.

SCREENING FOR FAMILIAL HYPERCHOLESTEROLAEMIA

K. Boregowda*, S. Rice, B. Grey, R. Bracken, J. stephens, S. Williams, M. Thomas, M. Williams.

Prince Philip Hospital, Llanelli, UK

* Corresponding author.

Hypercholesterolemia usually results from diet rich in saturated fatty acids combined with genetic predisposition. It can also be entirely secondary to genetic cause as in familial hypercholesterolemia (FH) which is characterised by premature coronary heart disease and/or tendon xanthoma. Currently universal screening for FH is not recommended in UK as the evidence shown was not cost effective. According to NICE criteria diagnosis of definite FH is made if the patient has elevated cholesterol levels(HDL more than 7.5 mmol/L or LDL more than 4.9 mmol/L) and tendon xanthoma, and a diagnosis of possible FH is made if the patient has elevated cholesterol levels as mentioned above and a family history of hypercholesterolemia or heart disease. Patients with possible FH are higher in UK population than definite FH. Possible FH may include some