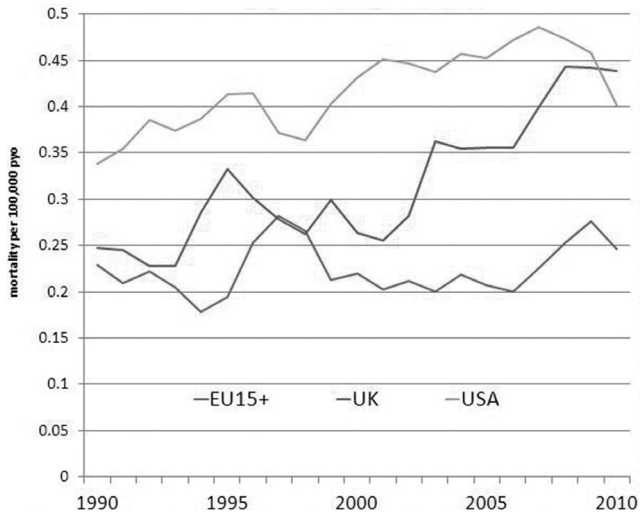
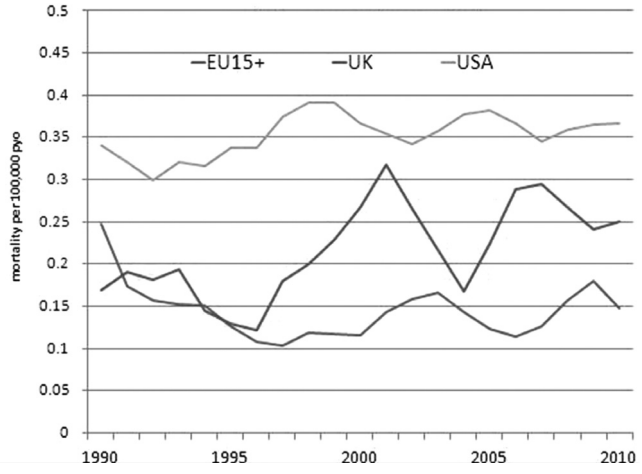


Abstract G476 Figure 2 Total diabetes mortality amongst 15–24 year males (3 year moving averages)



Abstract G476 Figure 3 Total diabetes mortality amongst 15–24 year females (3 year moving averages)

coefficient $p < 0.0001$) but rising mortality amongst 15–24 year olds (positive slope, $p < 0.0001$ both sexes).

Discussion Diabetes mortality in the UK for children 1–14 years approximates the EU15+ mean and is better than in the USA. However, for 15–24 year olds, the UK has high and rising diabetes mortality compared with the EU15+ from 2000 onwards. Further work is needed to understand the contributions of healthcare factors to the UK's poor diabetes mortality record amongst young people.

G477 IDENTIFICATION OF NOVEL PAR2 MUTATION IN THROMBOTIC MICROANGIOPATHY

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Atypical Haemolytic Uraemic Syndrome (aHUS) is a rare cause of renal failure, occurring as a result of glomerular endothelial cell injury, with a prevalence of 3–5 per million. The clinical features consist of recurrent episodes of haemolytic anaemia, thrombocytopaenia and renal failure with biopsy evidence of thrombotic microangiopathy.

Mutations in complement regulatory genes account for approximately 70% of cases. More recently, components of the coagulation cascade, such as DGKE, have been implicated in the aetiopathogenesis of aHUS. We have identified a novel mutation in protease–activated receptor 2 (PAR2) in a patient with an aHUS phenotype.

Methods Whole Exome Sequencing (WES) was performed on a child presenting at the age of 3 years with nephrotic range proteinuria and biopsy evidence of thrombotic microangiopathy, thrombocytopaenia and haemolytic anaemia. One year from presentation, his renal function recovered to baseline but he continues to experience episodic haemolytic anaemia and thrombocytopaenia. Of note, there is a familial history of relapsing thrombocytopaenia affecting the patient's father and aunt.

Results WES did not demonstrate any mutations in known aHUS genes. A novel mutations in PAR2 (Y345H) was identified, *in silico* analysis of this classified this as deleterious. This mutation was not detected in databases of healthy controls.

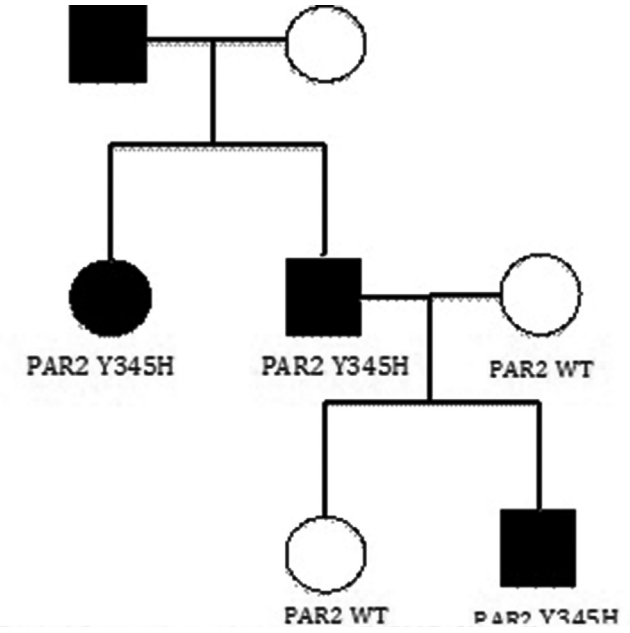
Sequence analysis demonstrated segregation in affected family members (Figure 1)

Western blot analysis suggests reduced PAR2 expression in the patient's serum compared to controls. We also show that PAR2 is expressed in glomerular cells (Figures 2 and 3)

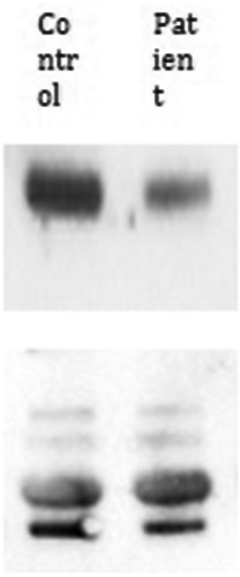
Discussion PAR2 is a G-protein coupled receptor, which is activated by a number of pro-inflammatory and coagulation mediators. Activation of this receptor causes a positive feedback loop, leading to a pro-thrombotic state that may result in pathological platelet activation and endothelial dysfunction. As there are high levels of PAR2 in the kidney, this pro-thrombotic state may lead to the thrombotic microangiopathy seen in aHUS.

PAR2 has additional roles in complement regulation that are less well defined. It is known to cause down–regulation of DAF, which is an important regulator of the complement pathway.

Further analysis of genetically undefined cases of TMA and MPGN are required for PAR2 mutational screening to determine



Abstract G477 Figure 1 Segregation analysis showing PAR2 Y345H in affected



Abstract G477 Figure 2 PAR2 expression in serum from control and patient samples

Abstract G477 Figure 3 PAR2 expression in immortalised kidney cells,demonstrating expression in wild-type endothelial,mesangial and podocyte cells

whether PAR2 represents a unique pathway in these rare renal phenotypes.

G478(P) A CASE REPORT OF TRBETA MUTATION LEADING TO RAISED T4 LEVELS

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Introduction We present a five year old girl with thyroid hormone resistance, subsequently discovered to be heterozygous for TRbeta mutation. This case highlights the necessity to investigate, in detail, all children with persistently high thyroxin with normal TSH levels in order to aid future management and the necessity to follow them up.

Case report The patient was born at term by normal delivery, weighing 3.34kg (50th centile). She was referred at six months of age for poor weight gain (2nd centile). Blood tests showed an elevated free T4 (43.4) with normal TSH (3.10). Systemic examination was normal and remained so over the following months. Repeat thyroid function tests showed persistently elevated T4 with normal TSH. At 2 ½ years old, genetic analysis revealed she is heterozygous for TRbeta mutation (thyroid hormone receptive gene). Mum has no mutation detected and her father cannot be tested for unavoidable reason. Since then, she has had slow growth, idiopathic thrombocytopenic purpura, vitamin D deficiency, and coeliac disease. Broader antibody testing has not revealed an underlying autoimmune aetiology to date. Recently, the patient has been investigated for recurrent falls and abnormal gait. She has right sided hemi hypotrophy with drooped shoulder and pelvis, along with winged scapulae, flared ribs and prominent abdomen. Her gross motor skills are generally delayed.

Conclusion Mutation of the beta thyroid hormone receptor is usually either autosomal dominantly inherited or is a *de novo* mutation, resulting in defective patterns of gene expression. This is a rare disorder, usually presenting with goitre. TRbeta mutation should be considered in children with persistently elevated T4 levels in conjunction with a normal TSH. The other immune conditions like ITP and changes in body habitus are new associations, cause of which is yet not identified. ** Photos are available **

G479(P) ADHERENCE TO BLOOD GLUCOSE MONITORING IN CHILDREN AND YOUNG PEOPLE WITH TYPE 1 DIABETES ON INSULIN PUMP THERAPY IN A TEACHING HOSPITAL

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Aims Children and young people with Type 1 diabetes on insulin pump therapy are expected to perform 4–8 capillary blood glucose (BG) tests per day for better glycaemic control. Our objective was to find out whether our patients adhered to the expected BG monitoring.

Methods Data was collected from 78 patients during a clinic visit over a period of one year. All children have glucometers which wirelessly transmits the data to their insulin pump. Average numbers of BG tests per day and mean BG levels were downloaded through the pump software for two weeks prior to their clinic visit.

Results 48 children (61.5%) did 4–8 BG tests per day while 18 (23.1%) did more than 8 tests. 12 (15.4%) who did less than 4 per day had a mean age of 14.8 years. We found moderately significant negative correlation between age and frequency of BG testing (Pearson's correlation coefficient (R) = –0.57) and also number of BG tests and mean BG levels (R=–0.52). There was a weak negative correlation between number of BG tests and HbA1c levels (R = –0.31). 5 patients (6.4%) entered fictitious BG levels manually into their pump and details are given in the table.