Case Report The index is a 2.5 year old girl with moderate eczema associated with nocturnal itch. She was referred to local services and was trialled on topical Clobetasone and Betamethasone cream. After little improvement this was changed to topical Hydrocortisone (1%) and Betamethasone cream. Her parents applied the steroid creams on a continuous basis for at least four months. They also sourced different homeopathic medicines from Pakistan. Upon analysis of their ingredients in the laboratory, Betamethasone and Dexamethasone were identified in one of them. She required a 5 day course of oral Prednisolone for an allergic reaction to nuts. Over time the eczema remitted but all treatments were continued. After six months, she presented with rapid weight gain over a 2 month period [weight >98th centile]. This was associated with increased skin pigmentation over ankles and knees, striae over her thighs and marked hypertrichosis.

Biochemical testing confirmed absence of diurnal variation with suppressed 8am cortisol levels. She was switched to maintenance eczema care with emollients and topical Tacrolimus. An ACTH stimulation test confirmed adrenal suppression [peak Cortisol 45nmol/L]. Adjunctive investigations for other causes of hypoadrenalism were reported normal. We educated the family on emergency management of cortisol deficiency and prescribed steroid replacement for emergency use only. After four weeks off all steroid containing medications, a repeat ACTH stimulation test confirmed normalisation of adrenal function [peak Cortisol 550nmol/L]. Four months later, her weight has normalised [75–91st centile] and her eczema has remained under control. The pigmentation and striae have faded and her hypertrichosis is no longer evident.

Discussion The role of corticosteroids in the management of inflammation is well established but has resulted in widespread, prolonged and often unsupervised use. There is inter-individual variation in steroid sensitivity, small doses can result in dramatic adverse effects. We did suspect that the homeopathic medicine was steroid based. This does not out-rule the possibility that the other ingredients facilitated steroid increased absorption or reduced metabolism.

Conclusion Adrenal suppression is a rare side effect of topical steroid use. Children on courses of steroids for longer than one week require medical monitoring to ensure that the treatment is appropriate, safe and used correctly.

P289 METABOLIC COMPLICATIONS OF OBESITY IN CHILDREN

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Introduction Children with obesity have high risk of metabolic complications.

Aim To reveal frequency of metabolic complications in children with obesity.

Methods We examined 91 obese children, aged 7–17 (BMI > 95 percentile). Mean age of children was 12.46 ± 3.5 yrs. Obesity in children manifested at 5.3±0.5 yrs. Family anamnesis characterized by obesity in 71%, diabetes type 2 - in 25%, hypertension - in 53% in the first degree relatives. All patients were examined by clinical, biochemical, ultrasound methods. An oral glucose tolerance test (OGTT) accompanied by four point of insulinemia was performed. HOMA index was calculated according to the standard formula. In children with fatty

liver chronic hepatitis were excluded. Metabolic syndrome (MS) was diagnosed according to a classical definition (Weiss's criteria).

Results In obese children metabolic complications were found in 39.6%. The prevalence of the metabolic complications was follows: hypertriglyceridemia 38.2%, glucose intolerance 17.6%, hypertension 52.6%. Increase of serum cholesterol was revealed in 24%, low density lipoproteins - in 14%, decrease of high-density lipoproteins - in 32% children. Metabolic syndrome was found in 18 (19.8%) patients with BMI 30.9 ± 3.4 kg/m². Insulin resistance revealed in 25% children. HOMA index was 4.6 ± 3.3 mIU/l. Ultrasound signs of fatty liver were shown in 40 patients.

Conclusions This study showed a high prevalence of metabolic complications among obese schoolchildren.

P290 POSSIBILITIES OF GENETIC RESEARCH IN THE PREVENTION OF THE DEVELOPMENT OF EXCESS MASS OF THE BODY AND OBESITY IN CHILDREN

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Relevance Conducting genetic research in pediatric practice can help to create personalized dietary and therapeutic recommendations, as well as the implementation of appropriate physical activity.

Objective To determine the presence of polymorphisms of genes that contribute to the development of excess fat mass, increase the speed of carbohydrate absorption in patients with overweight and obesity to create further personalized recommendations on diet therapy and physical activity.

Patients and methods Surveyed 9 children (3 boys and 6 girls) aged from 6 to 10 years. Anamnesis was collected, an objective examination of patients, a biochemical examination of blood (lipidogram, fasting glucose), and a hormonal examination (insulin, TSH) were performed. All children underwent genetic screening based on DNA analysis (material - buccal epithelium) with the definition of gene polymorphisms: the FABP2 gene, which regulates the rate of fat absorption; PPARG gene, affecting the growth rate of fat cells; gene ADRB2, affecting the rate of carbohydrate consumption in the blood during exercise; The TCF7L2 gene, which regulates insulin secretion rate when glucose is released.

Results 4 patients were overweight, grade 1 obesity - 2; 2 degrees - 2; Grade 3 obesity - 1 child. In all nine patients, unfavorable gene polymorphisms were found, contributing to impaired fat metabolism. In 5 children, according to DNA analysis, a reduced rate of consumption of carbohydrate reserves in response to an increase in the level of adrenaline in the blood was noted. 4 children showed a genetic predisposition to a decrease in the rate of insulin secretion in response to glucose intake. In a 3rd degree obese patient, all the studied gene polymorphisms that adversely affect carbohydrate and fat metabolism were found.

Conclusion All patients showed a genetic predisposition to impaired metabolism of fats and/or carbohydrates. Grade 3 obesity is associated with all modifications of genes that adversely affect both carbohydrate and fat metabolism, and

the effectiveness of physical activity. The presence in patients with obesity and overweight polymorphisms of genes that adversely affect carbohydrate and fat metabolism, dictates the need to organize a special personalized approach to diet therapy and exercise.

P291 NEPHROGENIC DIABETES INSIPIDUS IN A FEMALE INFANT

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Aim Nephrogenic Diabetes Insipidus (NDI) is rare. 90% of cases are due to a defect in the AVPR2 gene which is widely believed to be inherited in an X-linked recessive pattern; from asymptomatic carrier mothers, to severely affected sons, but not daughters. Other, less common cases (~1% of NDI cases), are inherited in an autosomal dominant pattern due to a defect in the AQP2 gene. However, our case will demonstrate how females can present with symptomatic NDI secondary to AVPR2 mutation.

Methods This is a case study of a 14-month-old girl who was referred to the Paediatric Outpatient Department with a history of faltering growth, excessive drinking and plentiful wet nappies. At birth she plotted on the 50th centile for weight but subsequently dropped to the 9th. Weaning was a difficult, with her preferring liquids to solids. Moreover, excessive thirst resulted in her drinking water from the swimming pool, bath water and even the dog's bowl. Serum electrolytes, in addition to serum and urine osmolality and a desmopressin test, confirmed the diagnosis of NDI.

There was positive family history with the patient's Father having NDI, treated initially with diuretics then desmopressin until age 14, and since no longer requiring medication. An assumption was made that the patient thus acquired NDI via autosomal dominant inheritance of AQP2 gene. However, genetic tests were not performed at this stage.

Results The patient's Father was found to be hemizygous for AVPR2 gene. Genetic testing then revealed the patient to be a carrier of AVPR2 gene. Inherited via X-linked recessive form this would not normally affect females. Nevertheless, due to lyonisation of X-chromosome this patient was symptomatic.

Conclusion X-linked autosomal recessive disorders can also affect females. This is due to the process of lyonisation, which in itself has different forms and causes. Appreciation of lyonisation defect is crucial in the diagnosis and family counselling of patients with X-linked recessive disorders such as NDI, in addition to other more common disorders such as Glucose-6-Phosphate Dehydrogenase Deficiency (G6PD), Duchenne Muscular Dystrophy or Haemophilia.

P292 NEONATAL DIABETES IN A TERTIARY CENTRE; GENETICS DICTATING MANAGEMENT

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Background Neonatal diabetes mellitus is a rare condition with one case per 300,000 to 500,000 live births. It presents with marked hyperglycaemia in the first six months of life and is commonly of generic origin. Approximately half of cases are transient (TNDM) with the remainder being permanent (PNDM). The majority of Permanent Diabetes Mellitus (PNDM) cases are secondary to genetic mutations in K-ATP channel genes.

Case We report two infants who presented in the neonatal period with hyperglycaemia and were subsequently diagnosed with neonatal diabetes.

The first infant presented at 22 hours of life with blood glucose of 44.3 mmol/L and in ketoacidosis. He was born by LSCS at 34 weeks gestation due to IUGR with a birth weight of 1.36 kg. He received an IV insulin infusion for two months with frequent dose titration due to challenging glycaemic control. He was then successfully transitioned to a subcutaneous insulin infusion pump. Genetic analysis confirmed homozygous INS non sense variant, p(Ar43Ter).

The second infant presented at six weeks of age in severe diabetic ketoacidosis with a blood glucose of 60 mmol/L. She was born at term weighing 2.46 kg following induction of labour for IUGR. She presented with lethargy and vomiting for 24 hours on a background of failure to thrive and chronic candidiasis from birth. She was managed with an IV insulin infusion in the ICU before transitioning to a subcutaneous insulin pump. Genetic analysis revealed a *de novo* KCNJ11 gene mutation. She was then successfully transitioned to oral Glibenclamide which optimised her glycaemic control and resulted in complete withdrawal of subcutaneous insulin.

Discussion These are two cases of NDM with identified genetic mutations. The INS mutation is localised to amino acid residues affecting cleavage and/or folding of pre-proinsulin and pro-insulin which leads to prolonged ER stress and subsequent B-cell apoptosis. The KCNJ11 gene mutation identified in our second patient results in K-ATP channel overactivity. The K-ATP channel is at the end of the glycolytic pathway and has a KIR amino terminus responsible for channel gating. Its deletion results in channels that are continuously closed reducing sensitivity to inhibitory ATP and resulting in dramatic hyperglycaemia. Oral glibenclamide inhibits K-ATP channel activity with resultant normoglycaemia. Early identification is essential for optimal management and targeted therapy.

P293 AN AUDIT OF PREGNANCY OUTCOMES IN WOMEN WITH CHILDHOOD ONSET TYPE 1 DIABETES MELLITUS

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Background Pregnancy in women with type 1 diabetes mellitus is associated with an increased risk of congenital malformations, obstetric complications, and neonatal morbidity. In order to minimise morbidity for both mothers and infants there needs to be good interdisciplinary care between diabetologists, obstetricians, neonatologists and relevant nursing specialists.