International Conference on Birth Defects
2014
“Genes, Genome and Human Malformations”
9 – 11 February 2014
&
Symposium on Genetic Eye Diseases in Clinical Ophthalmology
11 February 2014
Waters Edge, Colombo, Sri Lanka

PROGRAMME & ABSTRACT BOOK

Organised by
The Human Genetics Unit, Faculty of Medicine,
University of Colombo, Sri Lanka
in Collaboration with
The Indo-UK Genetic Education Forum, Wales Gene Park,
Cardiff University, Cardiff, UK
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MESSAGE FROM THE DEAN, FACULTY OF MEDICINE UNIVERSITY OF COLOMBO

It gives me great pleasure to welcome all of you to Colombo for this International Conference on Birth Defects 2014 - “Genes, Genome and Human Malformations”. We are particularly pleased, as this is the first time that a conference on birth defects has been organized in Sri Lanka. In this regard we wish to express our sincere thanks to Prof. Dhavendra Kumar who played a pivotal role in bringing this conference to our country. My thanks also go out to our very own, Prof. Vajira H. W. Dissanayake who has been responsible for all the innovative and original ideas and projects which he effortlessly brings to life.

Formal teaching and providing a genetic service to our citizens in Medical Genetics was introduced to Sri Lanka with the establishment of the Human Genetics Unit (HGU) of the Faculty of Medicine, University of Colombo in 1983. This landmark Conference, held during the 30th Anniversary year of the HGU, will further strengthen our resolve and be a source of great encouragement to us at the HGU in our quest to identify and prevent birth defects in Sri Lanka in the future.

While thanking the World Health Organisation [WHO] for highlighting the burden of birth defects, we wish to appreciate and laud the Ministry of Health for laying the foundation for initiating a Birth Defects Surveillance Programme in Sri Lanka.

The presence of so many specialists and scientists from overseas and our own country will certainly open new vistas in the firmament of birth defects, that will enable us to prevent and control their incidence and also educate and train our doctors to reduce this heavy burden of morbidity and mortality.

May this meeting in Colombo be a very stimulating, productive and eventful one, and I sincerely hope that it will be the forerunner to many such meetings in the years to come.

Professor Rohan W Jayasekara MBBS, PhD (N.Cle’. U.K.), C.Biol., MSB (Lond)
Founder Director, Human Genetics Unit
Dean, Faculty of Medicine
University of Colombo
Sri Lanka
MESSAGE ON BEHALF OF THE INDO-UK GENETIC EDUCATION FORUM

On behalf of the Indo UK Genetic Education Forum, I am very pleased to welcome you to this major initiative for the first time in Sri Lanka. I am grateful to Prof. Vajira H. W. Dissanayake and his colleagues in the University of Colombo and the Human Genetics Unit for the kind invitation and hosting this great event in fabulous venue. This is truly like dream come true.

The Indo-UK Genetic Education Forum is a voluntary effort by members of the UK genetic/genomic medicine community (human geneticists, clinical geneticists, laboratory geneticists and genetic/genomic academicians and researchers) who wish to engage with genetic professionals and specialist clinicians in the Indian subcontinent and South East Asia with the sole of aim of enhancing and improving the status of genetic and genomic medicine and education across the whole region.

The Forum has organised several symposia and seminars across India since 2010. On each occasion we chose a specific area or field of specialist interest and engaged with most closely associated genetic and specialist clinicians. So far we have focused on general clinical genetics, cardiovascular genetics, congenital anomalies and clinical dysmorphology, fetal and prenatal medicine, cancer genetics and genetic and genomic technologies in medicine and health. The Forum aims to expand into core medical and biomedical sciences and encourage young generation of doctors and scientists to develop skills in genetics and genomics. There is no doubt that the future of medicine and health practices and biomedical science related professions would largely depend on innovative and applied genetic and genomic research and education.

The Organising Committee and the Faculty decided to focus on congenital anomalies in a general way highlighting the current clinical and laboratory practices in the diagnosis and prevention of congenital malformations and dysmorphic syndromes encompassed in the specialist field of clinical dysmorphology. In addition, we have selected genetic and inherited eye diseases as a specialist field. This reflects growing awareness and need to make early diagnosis and management of a number of eye conditions (in addition to dietary deficiencies and communicable infections) that collectively cause a huge burden of family, community and global blindness as recognised by the World Health Organization.

The three day programme is delivered by a joint dedicated Faculty drawn from UK, Sri Lanka and India. The Faculty reflects wide spectrum with a special knowledge and interest in birth defects and genetic/inherited eye disorders. The programme has been approved for 18 hours credit by the Royal College of Physicians in London for Continued Professional Development (Continued Medical Education) that is equivalent and transferable by any professional group worldwide for the purpose of CME.
On behalf of the Programme and Organising committee I am grateful to all of you for your interest and participation in this important joint Indo-UK-Sri Lanka educational and professional event. I hope you will find this enjoyable, stimulating and opportunity for networking and building new professional relationships.

Best wishes and warm regards

Professor Dhavendra Kumar MD, FRCP, FRCPI, FRCPCH, FACMG
Chair and Co-ordinator, Indo-UK Genetic Education Forum
Director, International Programme, The Wales Gene Park, Cardiff University, UK
Consultant Clinical Geneticist/Cardiovascular Genetics, Institute of Medical Genetics, University Hospital of Wales, Cardiff, UK
MESSAGE ON BEHALF OF THE SRI LANKAN HOSTS

It gives me great pleasure to welcome all of you to this first ever Birth Defects Conference in Sri Lanka. Like many such endeavours, with this conference, the march towards reducing birth defects in Sri Lanka has begun with a small band of committed individuals spurred on by friends and colleagues from overseas who have had vast experience in the field in their own countries.

The dramatic reduction in infant and neonatal mortality in Sri Lanka during the past few decades has brought Sri Lanka’s neonatal and infant mortality indicators within reach of Western figures. Today what is preventing us from achieving Western figures is the considerable contribution that birth defects make to neonatal and infant mortality. The figure could be as high as 20%. The time has come therefore to address the issue urgently.

In this background highlighting the burden of birth defects, equipping doctors with knowledge to deal with birth defects, and rallying all stakeholders to make a concerted effort towards reducing birth defects is very important. This conference aims to do that.

I wish to thank Prof. Dhavendra Kumar who has been encouraging us all the way and supporting us by bringing the ‘full force’ of the Indo-UK Genetic Education Forum to Colombo. I wish to thank our colleagues from the UK and India who have taken time off from their busy schedules to come over to share their expertise with us.

The burden of birth defects is not something unique to Sri Lanka. It is a burden shared by all countries in the region. I am particularly pleased that we were able to support our colleagues from Pakistan, Maldives and Nepal to attend this conference. I hope that they will go back home with a renewed commitment to reduce birth defects in their countries, and that we will be able to help them in their endeavours in the years to come.

The countries in the region have rallied around under the banner of the World Health Organisation (WHO) for action aimed at reducing birth defects in the region following the resolution at the World Health Assembly calling on member states to take action to reduce birth defects. I applaud the leadership taken by the WHO which has strengthened our hands.

I wish you all a memorable conference.

Professor Vajira H. W. Dissanayake MBBS (Colombo), PhD (Nottingham), FNASSL
Professor, Human Genetics Unit
Faculty of Medicine
University of Colombo
Sri Lanka
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<td>Prof. Rohan W. Jayasekara</td>
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<td>Director, Human Genetics Unit and Dean, Faculty of Medicine, University of Colombo</td>
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<td>Dr. Firdosi Rustom Mehta</td>
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<td>Genes, Genomes and Birth Defects: The Ciliopathies</td>
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<td>Professor of Medical Genetics and Consultant Clinical Geneticist</td>
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<td>Institute of Child Health, University College London; Guy’s Hospital, London; and Great Ormond Street Hospital, London.</td>
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<td>Prof. Vajira H. W. Dissanayake</td>
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**Chairs: Prof. Veronica van Heyningen (UK) and Prof. Rohan W. Jayasekara (Sri Lanka)**

**Introduction to Congenital Anomalies and Clinical Dysmorphology**
Sarah Smithson, Bristol, UK

**Molecular Basis of Birth Defects**
Dhavendra Kumar, Cardiff, UK

**Laboratory Diagnosis in Clinical Dysmorphology**
Daniela Pilz, Cardiff, UK

**Birth Defects Surveillance Programme in Sri Lanka**
Kapila Jayaratne, Colombo, Sri Lanka
13.00  Lunch & Lunch Time Symposium

Chairs: Neil Seneviratne (Sri Lanka) and Duminda Samarasinghe (Sri Lanka)

Genetics Services in a Maternity Hospital in Sri Lanka
Padmapani Padeniya, Colombo, Sri Lanka

Genetic Services in a Cardiology Unit in a Children’s Hospital in Sri Lanka
Subhashi Karunaratne, Colombo, Sri Lanka

14.00  Session II: Fetal Perspectives of Birth Defects

Chairs: Georgina Hall (UK) and Ratna Puri (India)

Antenatal Diagnosis of Fetal Anomalies
Tiran Dias, Colombo, Sri Lanka

Congenital Malformations at Necropsy Examinations:
The Past Experience: Chandu De Silva, Colombo, Sri Lanka
The Current Experience: A. A. H. Priyani, Colombo, Sri Lanka

Fetal and Neonatal Growth Disorders - Approach and Diagnosis
Trevor Cole, Birmingham, UK

15.30  Tea

16.00  Session III: Dysmorphology Workshop

Facilitators: Sarah Smithson, Daniela Pilz, Ruwangi Dissanayake

The London Dysmorphology Database
Interactive Session and Selected Case Presentations

17.30  Welcome Reception
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<td>09.00</td>
<td>Session IV: Cranio-Facial and Related Anomalies</td>
<td>Chair: Philip Beales (UK) and Saqib Mahood (Pakistan)</td>
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<td></td>
<td>Clinical and Molecular Approach to Craniosynostosis and Related Disorders</td>
<td>Sarah Smithson, Bristol, UK</td>
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<td>Oro-facial Clefts – Clinical and Genetic Perspectives</td>
<td>Sheetal Sharda, Chandigarh, India</td>
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<td>Orofacial Clefts in Sri Lanka</td>
<td>Sanath P. Lamabadusuriya, Colombo, Sri Lanka</td>
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<td>Session V: Brain and Spinal Cord Malformations</td>
<td>Chairs: Graeme Black (UK) and Dulika Sumathipala (Sri Lanka)</td>
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<td></td>
<td>Overview and Classification of Brain and Spinal Cord Malformations</td>
<td>Dhavendra Kumar, Cardiff, UK</td>
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<td>Lissencephaly, Holoprosencephaly and Related Brain Malformations</td>
<td>Daniela Pilz, Cardiff, UK</td>
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<td>Molecular Diagnosis in Brain and Spinal Cord Malformations</td>
<td>Philip Beales, London, UK</td>
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<td>12.30</td>
<td>Lunch &amp; Lunch Time Symposium</td>
<td>Chairs: Vajira H. W. Dissanayake (Sri Lanka) and Manouri Senanayake (Sri Lanka)</td>
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<td>Thalassaemia - The Current Status in Sri Lanka</td>
<td>Palitha Maheepala, Colombo, Sri Lanka</td>
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<td>Bone marrow Transplantation for Thalassaemia</td>
<td>Lallindra Gooneratne, Colombo, Sri Lanka</td>
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<td>13.30</td>
<td>Session VI: Skeletal Dysplasias and Related Disorders</td>
<td>Chair: Daniela Pilz (UK) and Udari Liyanage (Sri Lanka)</td>
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<td>Classification and Clinical Approach to Skeletal Dysplasias</td>
<td>Trevor Cole, Birmingham, UK</td>
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| 15.30  | **Session VII: Malformations in Inherited Metabolic Diseases**  
*Sponsored by Genzyme*  
Chairs: Sarah Smithson (UK) and Sheetal Sharda (India)  
Treatable Lysosomal Storage Disorders - Diagnosis and Management  
Ratna Puri, New Delhi, India  
Initial Experience of Enzyme Replacement Therapy in Gaucher Disease  
Roshini Karunanayake, Colombo, Sri Lanka  
My Journey with Gaucher Disease  
Suyog Sathe, LSDSS Representative |
| 17.00  | Close                                        |
| 19.30  | **Faculty Dinner**  
*Sponsored by Genzyme* |
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<td><strong>Session VIII: Congenital Ocular Anomalies</strong></td>
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<td>Chairs: Dhavendra Kumar (UK) and Lalitha Senarath (Sri Lanka)</td>
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<td><strong>Introduction - Spectrum and Epidemiology of Genetic Eye Diseases</strong></td>
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<td>Graeme Black, Manchester, UK</td>
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<td><strong>Anophthalmia, Microphthalmia and Coloboma - Genetics to Biology</strong></td>
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<td>Veronica van Heyningen, Edinburgh/London, UK</td>
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<td><strong>Lenticular Anomalies and Anterior Chamber Anomalies</strong></td>
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<td>Veronica van Heyningen, Edinburgh/London, UK</td>
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<td><strong>Vitreous, Choroidal and Retinal Disorders</strong></td>
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<td>Chairs: Philip Beales (UK) and Nilam Thakur (Nepal)</td>
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<td><strong>Vascular Complications in Inherited Connective Tissue Disorders</strong></td>
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<td>Dhavendra Kumar, Cardiff, UK</td>
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<td><strong>Neoplasia in Clinical Dysmorphology</strong></td>
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<td>Trevor Cole, Birmingham, UK</td>
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<td><strong>Renal and Genito-Urinary Anomalies</strong></td>
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<td>Malik Samarasinghe, Colombo, Sri Lanka</td>
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<td>Chairs: Rohan W. Jayasekara (Sri Lanka) and Vajira H. W. Dissanayake (Sri Lanka)</td>
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<td><strong>Neurogenetics in Sri Lanka</strong></td>
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<td>Dulika Sumathipala, Colombo, Sri Lanka</td>
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<td><strong>Disorders of Sexual Development in Sri Lanka</strong></td>
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<td>Nirmala Sirisena, Colombo, Sri Lanka</td>
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<td>Session X: Management of Congenital Anomalies and Dysmorphic Conditions</td>
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<td>Chairs: Daniela Pilz (UK) and Nirmala Sirisena (Sri Lanka)</td>
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<td>Multi-Disciplinary Endocrine Genetic Service - Disorders of Sexual Development</td>
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<td>Trevor Cole, Birmingham, UK</td>
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<td>Genetic counselling issues in Clinical Dysmorphology</td>
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<td>Sarah Smithson, Bristol, UK</td>
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<td>Prenatal and Pre-implantation Genetic Diagnosis</td>
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<td>Georgina Hall, Manchester, UK</td>
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<td>Fetal Surgery for Birth Defects</td>
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<td>Nalinda Rodrigo, Colombo, Sri Lanka</td>
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SYMPOSIUM ON GENETIC EYE DISEASES
IN CLINICAL OPHTHALMOLOGY
PROGRAMME
TUESDAY, 11 FEBRUARY 2014

08.30  Registration

09.00 Joint Session VIII & Session I: Congenital Ocular Anomalies

Chairs: Dhavendra Kumar (UK) and Lalitha Senarath (Sri Lanka)

Introduction - Spectrum and Epidemiology of Genetic Eye Diseases
Graeme Black, Manchester, UK

Anophthalmia, Microphthalmia and Coloboma - Genetics to Biology
Veronica van Heyningen, Edinburgh/London, UK

Lenticular Anomalies and Anterior Chamber Anomalies
Veronica van Heyningen, Edinburgh/London, UK

Vitreous, Choroidal and Retinal Disorders
Philip Beales, London, UK

Inherited Corneal Disorders
Graeme Black, Manchester, UK

11.00 Tea/ Coffee

11.30 Session II: Clinical Ophthalmic Genetics

Chairs: Veronica van Heyningen (UK) and Champa Banagala (Sri Lanka)

Genetic Clinics for Ophthalmology
Daniela Pilz, Cardiff, UK

Gene Identification in Genetic Eye Disorders
Graeme Black, Manchester, UK

Genetic Counselling in Ophthalmology
Georgina Hall, Manchester, UK

13.00 Lunch

Join the Lunch Time Symposium in ICBD 2014
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<td>14.00</td>
<td>Session III: Ophthalmic Genetic Disorders</td>
<td>Ocular Manifestations of Ciliary Disorders (Ciliopathies)</td>
<td>Philip Beales, London, UK</td>
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<td>Metabolic and Mitochondrial Genetic Eye Diseases</td>
<td>Dhavendra Kumar, Cardiff, UK</td>
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<td>Retinoblastoma and Other Paediatric Genetic Eye Diseases</td>
<td>Trevor Cole, Birmingham, UK</td>
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<td>16.00</td>
<td>Session IV: Ophthalmic Genetics in Clinical Medicine</td>
<td>Clinical Genetic Testing for Genetic and Inherited Ophthalmic Disease</td>
<td>Georgina Hall, Manchester, UK</td>
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<td>Recent Developments and Directions in Ophthalmic Genetic Research</td>
<td>Veronica van Heyningen, Edinburgh/London, UK</td>
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<td>The Future of Genetic and Inherited Eye Disease - New Diagnostic and Therapeutic Approaches</td>
<td>Graeme Black, Manchester, UK</td>
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**UNITED KINGDOM**

**Prof. Philip Beales** BSc MD FRCP FMedSci

Philip Beales is Professor of Medical Genetics at the Institute of Child Health, University College London, and a Consultant Clinical Geneticist at Guy's Hospital and Great Ormond Street Hospital in London. His research is focused on the study of the role of primary cilia in disease and development. He has a longstanding interest in the ciliopathy Bardet-Biedl Syndrome, and his laboratory was instrumental in unveiling the role of primary cilia dysfunction in the pathogenesis of this rare congenital condition.

He also discovered that the aetiology of a group of skeletal disorders such as Jeune Asphyxiating Thoracic Dystrophy, Craniocutaneous Dysplasia, and Acrocallosal syndrome also involves primary ciliary dysfunction. One of the key goals of his laboratory is to identify targets for therapy in ciliopathies through the understanding of the role of primary cilia in disease.

Professor Beales is Medical Advisor to the Laurence-Moon-Bardet-Biedl Society in the UK, and is a founder member of Ciliopathy Alliance UK, which comprises patient organisations, medical researchers, physicians, and other healthcare professionals representing individuals and families affected by diseases associated with ciliary dysfunction.

p.beales@ucl.ac.uk

**Prof. Graeme C.M. Black** DPhil, FRCOphth

Graeme Black is Professor of Genetics and Ophthalmology at Central Manchester University Hospitals NHS Foundation Trust. During training he undertook at DPhil with Professor Ian Craig in the Department of Biochemistry at the University of Oxford, studying the genetics of X-linked inherited ophthalmic disease. It was this period that enabled him to develop his combined subspecialty interests.

Having moved to Manchester in 1995 Graeme became a Wellcome Trust Clinician Scientist Fellow in 1997 and a Wellcome Trust Senior Research Fellow in 2002. This enabled him to focus on functional analyses of recently identified genes, defining their role in normal development as well as in the disorders studied. Graeme was the director of the NIHR Manchester Biomedical Research Centre (BRC), a specialist centre in Genetics and Developmental Medicine, from 2009-2012. Graeme lead the BRC to develop an impressive track record of translating scientific breakthroughs into clinical practice.

In 2012 Graeme became the director of the Institute of Human Development, within the Faculty of Medical and Human Sciences at The University of Manchester. The Institute brings together research in the areas of genetic medicine, specialist senses, diabetes & endocrinology, maternal and fetal health and paediatrics.

Graeme's major research interest is the investigation of genetic disorders associated with visual disability. The ultimate aims are to improve the diagnosis, management and treatment of such conditions. This work has focused on the characterisation of genes and proteins underlying inherited developmental disorders such as anophthalmia, cataract and retinal degenerative disorders.
Graeme oversees a scientific team that provides genetic testing for retinoblastoma, the commonest ocular malignancy of childhood. Furthermore, through funding provided by the Department of Health and the British Retinitis Pigmentosa Society his team has developed a national genetic testing service for inherited retinal diseases. These include several forms of retinitis pigmentosa, cone-rod dystrophy as well as a number of macular dystrophies.

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Dr. Trevor Cole MB,ChB, FRCP

Consultant in Clinical and Cancer Genetics at the Birmingham Women’s Hospital Foundation Trust and Honorary Reader in Medical Genetics at the University of Birmingham. After training in adult medicine and paediatrics he worked as an Action Research Fellow and Specialist Registrar at the Institute of Genetics in Cardiff and as a Pathology Society Travel Fellow at the Research Institute in Toronto before his consultant appointment in Birmingham in 1992. His early research focused on genetic growth and endocrine disorders and this is now a significant component of his specialist work, and is the topic for over a third of 130 peer reviewed papers.

Consultant sabbatical periods at Oregon Health and Science University and Cedars Sinai in Los Angeles were spent in the fields of endocrine genetics and the International Skeletal Dysplasia Registry and he manage a large practice in these areas in joint multi-disciplinary regional or supra-regional clinics. Specific clinics cover areas including endocrine tumour syndromes and DSD disorders. He is also part of the multi-disciplinary team managing over half the cases of retinoblastoma in the UK, and work closely with paediatric oncology colleagues in the management of rare paediatric cancer syndromes.

As lead for cancer genetics services in the 1990’s his team developed and implemented clinical pathways for the management of inherited cancers and integrated molecular testing to improve the efficacy of management. A model since adopted by other units in the UK. As clinical lead for clinical genetics this remit expanded to include integration of medical genetics into a wide range of mainstream specialities. This pilot work was supported by an award of ½ million pounds by the Department of Health following the 2003 government white paper on medical genetics. This project focused on cardiac, endocrine and renal genetics. An additional clinical interest lies in the area of translational research and introduction of new genetic technologies into mainstream practice. Currently he is the joint Wellcome DH HICF award recipient to develop free fetal techniques for non invasive prenatal diagnosis for rare diseases.

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In addition to his professional commitment to clinical genetics & cardiovascular genetics, he is passionate for the applications of genomics in medicine, public/population health and biotechnology/bio-economy. He actively pursues promotion and collaboration for genetics/ genomics in healthcare and socio-economic benefits across the developing world through establishing professional networks of joint public-private partnership. He is one of the advisors to the WHO program for genomics in developing countries. He founded and leads the Indo-UK Genetic Education Forum and actively involved with similar initiatives for Africa, Asia-Pacific and Latin America.

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Prof. Daniela Pilz is a Consultant in Medical Genetics at the Institute of Medical Genetics, University Hospital of Wales, Cardiff. She graduated from Medical School in Hannover, Germany, and trained in paediatrics and clinical genetics in the UK. The topic of her MD thesis was "Lissencephaly". She spent 2 years as a research associate in a molecular laboratory at the University of Chicago in the Department of Human Genetics working on cortical malformations, specifically the molecular causes of the classical lissencephaly spectrum. Her clinical expertise lies in dysmorphology and paediatric neurogenetics. She currently leads a research programme into causes of cortical brain malformations.

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Dr Sarah Smithson is a Consultant in Clinical Genetics, Clinical Genetics Unit, St. Michael's Hospital, Bristol, UK. She has a background in hospital paediatric medicine and has worked in clinical genetics for more than 20 years. She has an interest in genetically determined craniofacial disorders and skeletal dysplasias and has contributed to research in both fields. She is involved in medical education and has been an organiser and Faculty member of numerous postgraduate meetings relating to clinical genetics. She is currently Chairman of the committee at the Royal College of Physicians in London which oversees the training of Clinical Geneticists in the UK.

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Prof. Veronica van Heyningen CBE, FRS, FRSE, FMedSci

Prof. Veronica van Heyningen is Honorary Professor and Visiting Scientist at MRC Human Genetics Unit, MRC IGMM, University of Edinburgh and Institute of Ophthalmology, University College London. Her first degree is in genetics (Cambridge); and her DPhil on early gene mapping studies using somatic cell hybrids, with Walter Bodmer (Oxford); She was a Beit Memorial Fellow in the MRC Mammalian Genome Unit, Edinburgh. Subsequently she rose through the ranks at MRC Human Genetics Unit, Edinburgh from postdoctoral fellow to group leader and until recently Section Head. Veronica has been an Honorary Professor University of Edinburgh and elected a Fellow of the Royal Society of Edinburgh, the Academy of Medical Sciences and in 2007 of the Royal Society. She was also a Howard Hughes International Research Scholar 1993-1998; Member of UK Human Genetics Commission 2000-2005; EMBO member 2003. She was made a CBE in 2010.

Human geneticist (non-clinical) working on developmental eye anomalies such as aniridia and anophthalmia/microphthalmia. Interested in what detailed analysis of the human phenotypes in individuals with known mutations can tell us about the biological role of the genes involved. Ultimately most human developmental genes need to be explored in model systems and we are currently studying the roles of PAX6 and SOX2 in humans, mice and zebrafish. A major area of endeavour, since the early 1990s, has been to understand the mechanisms of long-range regulation of gene expression. Transcription factors like PAX6, SOX2 and OTX2 show complex spatiotemporal and quantitative control of expression, requiring a large number of strongly sequence-conserved cis-regulatory elements, found upstream, downstream and within the gene. Such regulatory regions can stretch over more than a megabase either side of the gene. We are aiming to understand the spatial and functional organisation of these interacting elements (which often function as enhancers in reporter transgenic assays in mouse and zebrafish), additively recapitulating the sum of the total gene expression pattern. Expression-associated patterns of open chromatin suggest dynamic genomic organisation. Another emerging interest is in the mechanisms underlying disease with non-Mendelian segregation patterns often through non-penetrance. Her lab has also explored how other genes and environmental factors affect phenotype variation.

Veronica retired at the end of 2012 and is now an Honorary Professor and Visiting Scientist in both the MRC Human Genetics Unit of the IGMM at the University of Edinburgh and also at University College London and at the Institute of Ophthalmology.

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Dr. Ratna Dua Puri did her M.D. Pediatrics from Armed Forces Medical College, Pune and D.M. Medical Genetics from Sanjay Gandhi Institute of Medical Sciences, Lucknow. She has also attended many workshops and received additional training in Genetics at Paris, Manchester, Shenzhen, Taiwan and Hong Kong. Presently, she is a Senior Consultant and Vice Chairperson at the Center of Medical Genetics, Sir Ganga Ram Hospital, New Delhi.

She has got Dharam Vira Award of Excellence for Senior Officer in recognition of meritorious service rendered to the Hospital during the year 2010, and "Young Investigators Award" at the International Congress of Inborn Errors of Metabolism held in Tokyo, Japan from 12-16th September 2006 for the paper "Spectrum of Urea Cycle Disorders in the Indian population and prenatal diagnosis". Dr. Puri was the representative from India for deliberations at the Joint World Health Organization and MOD Meeting on Management of Birth Defects and Hemoglobin Disorders in Geneva in May 2006.

She is a member of the Editorial Board of Indian Journal of Pediatrics, Past Secretary of the Delhi Society for Prenatal Diagnosis & Therapy (DESPAT), Treasurer of Society of Fetal Medicine, Joint Treasurer of the Indian Society of Inborn Errors of Metabolism, and has also been the Secretary of the Genetics sub specialty chapter of the Indian Academy of Pediatrics. She is a member of the Task Force on Birth Defect Registry in India and Lysosomal Storage Disorders task force, an initiative of the Indian Council of Medical Research.

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P1: A case report of a Sri Lankan child with mosaic cell lines for ring chromosome 6 and monosomy 6

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Ring chromosome 6 is a very rare but well documented structural chromosomal anomaly with a varied phenotype. Literature rarely reveals autosomal monosomy compatible with life. In our case it could be the low grade mosaicism of monosomy 6 cell line that contributed to the resulting live birth. We describe a Sri Lankan girl mosaic for ring chromosome 6 and monosomy 6.

A thirteen year old girl born to a non consanguineous couple presented with dysmorphic features, short stature and severe pulmonary hypertension. She was delivered by an elective Caesarian section with a birth weight of 1.8 kg. She was treated with phototherapy for neonatal jaundice. She had delayed motor milestones and a significant speech delay during infancy and early childhood. At presentation her weight, height and head circumference were well below the third centile. She had a broad nasal bridge, microstomia, short neck, low posterior hair line, broad chest, fifth digit clinodactyly and bilateral wide sandal gap. Her breast development was compatible with Tanner's stage 1. She had very dry skin with ichthyosis. Echocardiographical studies found a structurally normal heart despite having severe pulmonary hypertension. Poor social interactions and age inappropriate behavior were also noted.

The karyotype in peripheral blood lymphocytes was 46,XX,r(6)(p25q27)[36]/45,XX,-6[4]. Karyotypes of the parents were normal. The chromosome aberration is therefore a postzygotic de novo mutation. Breakpoint analysis of adjoining ends of ring chromosome 6 using molecular cytogenetic studies has been arranged to further characterize the ring chromosome.

P2: A case report of a child with trisomy 21 and reciprocal translocation between chromosome 1 and 18

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One of the most common numerical chromosome abnormalities, Down syndrome also known as trisomy 21 is a genetic disorder that causes mental retardation, developmental delay and distinct dysmorphic features with an estimated incidence of 1 in 1000 births worldwide. Depending on the severity of the syndrome problems in development could range from moderate to severe.

We describe a case of a 4 months old male infant with features suggestive of Down syndrome. The patient was born at 37 weeks by breech vaginal delivery with a birth weight of 1.8 kg to a non-consanguineous couple. Patient has a 3 year old healthy male sibling. Clinical features such as hypotonia, hypertelorism, epicanthal folds, flat nasal bridge, atrial septal defect, bilateral simian crease and sandal gap were present at presentation. Chromosome culture and karyotyping of the peripheral blood lymphocytes of the patient indicated that apart from the presence of an extra copy of the chromosome 21, a translocation between chromosome 1 and 18 t(1;18)(q41;q12.1) was also present. Based on literature, other than features of Down syndrome such a patient should manifest clinical features of chromosome 18q- syndrome or chromosome 1q syndrome if the detected translocation is unbalanced. Since many clinical features overlap with the features of Down syndrome in order to determine exact phenotype-genotype correlation further studies will be carried out first by karyotyping the parents to exclude the possibility of inheriting a balanced translocation; if not by breakpoint analysis using molecular cytogenetic studies to detect the disrupted genes at the translocation breakpoints.
P3: A ring chromosome 18 in a Sri Lankan female child with congenital malformations and global developmental delay

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Ring chromosome 18 (r(18)) is a rare chromosomal abnormality which shows a varied phenotype. This is generally associated with developmental delay, mental retardation, hypotonia and facial dysmorphism. We report a two years old Sri Lankan female child presenting with dysmorphic features, global developmental delay, complex cyanotic heart disease, severe growth retardation and hypotonia. She was born to a non consanguineous couple after an uneventful pregnancy with all birth parameters below the third centile. Family history indicates an older healthy brother, followed by a spontaneous miscarriage at 8 weeks of gestation.

At presentation her weight and height was 4.5 kg and 59 cm respectively, with a head circumference of 39.5 cm. Distinct dysmorphic features were telecanthus, epicanthic folds, slightly up slanted palpebral fissures, microcephaly, flat occiput, flat nasal bridge, mid face hypoplasia, micrognathia, complete left sided cleft lip and cleft palate, low set ears, long tapering fingers and bilateral talipes equinovarus deformity. Routine G band karyotyping was performed and revealed a r(18) in all analyzed chromosome spreads. Both parents were karyotyped and found to be normal. Hence the abnormality detected in the child was concluded to be a de novo aberration.

Phenotype of patients with r(18) depends on the extent of the deleted chromosomal segments. Further molecular cytogenetic studies will be performed to identify the exact breakpoints of the terminal ends of the chromosome 18 to generate an exact phenotype-genotype correlation.

P4: Hypergonadotrophic hypogonadism associated with 46,X,inv(X)(p11.2p21)

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We report a 16 year old female diagnosed with primary amenorrhea. She was born as the fourth child of a non consanguineous 29 year old mother and 39 year old father. Family members other than the patient were phenotypically normal. Her reports indicate poor height and weight gain since early childhood. At the age of 16 years her height and weight were 128 cm and 28 kg respectively, with no secondary sexual characteristics. She had normal intellectual ability. Some minor dysmorphic features including broad chest, widely placed nipples and wide sandal gap were observed. Endocrine studies showed hypergonadotrophic hypogonadism with elevated levels of FSH (134.7 mIU/ml), LH (34.9 mIU/ml) and decreased levels of Oestradiol (11 pg/ml). Chromosome culture and karyotyping was performed with 72 hour stimulated culture followed by GTL banding. All the analyzed metaphases indicated an inversion of one of the X chromosomes with breakpoints at p11.2 and p21: 46,X,inv(X)(p11.2p21). Parents' karyotypes were normal, suggesting that it was a de novo aberration. The patients' phenotype may have been caused by a disturbed gene at region Xp11.2 or Xp21 as the break points lie across this region. A similar aberration has been reported in the literature with disruption of the upstream regulatory element of the NR0B1 gene located in the Xp21.2 region. It has caused adrenal hypoplasia with hypogonadotrophic hypogonadism in certain male subjects. Therefore further studies would be done to characterise this aberration further.
P5: Sex differences in the prevalence of congenital anomalies: A population-based study

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Background: Limited data is available concerning the sex distribution of various congenital anomaly subtypes. This study investigated sex differences in the prevalence of congenital anomalies, overall and by subtype, using high quality population-based data from the North of England.

Methods: Information on congenital anomalies occurring among singleton pregnancies during 1985–2003 was extracted from the Northern Congenital Abnormality Survey (NorCAS). Anomalies were categorized by groups, subtypes, and syndromes according to the European Surveillance of Congenital Anomalies guidelines. Relative risks (RRs) comparing the prevalences in males to that in females were calculated for a range of congenital anomaly subtypes.

Results: A total of 12,795 eligible cases of congenital anomaly were identified during the study period, including 7019 (54.9%) males and 5776 (45.1%) females. Overall, male fetuses were significantly more prevalent in pregnancies affected by a congenital anomaly than female fetuses (RR, male vs. female = 1.15; 95% confidence interval [CI], 1.11–1.19), but there was significant heterogeneity between subtypes (p < 0.001). Forty-four of 110 (40%) unique subtypes were at least 40% more prevalent in males than females, with affected subtypes occurring across all major anomaly groups. Thirteen of 110 (12%) unique subtypes were at least 40% more prevalent in females than males, but the female-biased RR of a neural tube defect was less pronounced than previously reported (RR = 0.84; 95% CI, 0.73–0.95).

Discussion: This study adds to the growing evidence of sex-specific differences in the prevalence of a wide range of congenital anomaly subtypes.

Acknowledgement: NorCAS is funded by the Healthcare Quality Improvement Partnership.

P6: Goitre genesis, mutagenesis and autoimmunogenesity of dioxins and related congeners: an experimental, retrospective, data review based study.

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Objectives: (1) To review Dioxin levels in Sri Lankan fish (2) To test the hypothesis of Goitre genesis, Mutagenesis and Autoimmunogenesity of the Dioxins and related Congeners

Introduction: A national survey conducted in 2005 showed hypothyroidism, thyroid diseases to be prevalent in the North Western Province (NWP) in spite of high Iodide concentration in drinking water, soil and small fish. It is major public health problem. The goiter rate is 3.8% to 4.9%. and goiters are present in 88% of hypothyroid patients.

Methodology: A convenience sample from General hospital Chilaw and Base hospitals of the Putalum district and Base Hospital Kulyapitiya from Kurunagala district recruited 672, 1702 and 506 patients respectively. A questioner was used as the study instrument. This was used to explore food behavior patterns.

Results: Poly Fluoro Chloro Phenols, Poly Fluoro Hexa Phenols, Coplanars are the highest concentration of PFO in marine brackish water fish. The concentrations are 123pg/g. in Chunn Strita and Thilapia notilica and in Thilapia mozambica, it was 11220pg/g. PFOS in marine fish Lathrinus leatjan was 281pg/g and 310pg/g, in Signus virgatus. Consumption of Iodide salt was 100% and fish 100%. However prevalence of goiters was 38%, thyroid cancer 9% of Base Hospital Kulyapitiya and Autoimmune thyroiditis was present in 38% of patients in General Hospital Chilaw.

Conclusions: PFOS in aquatic environment Sri Lanka is wide spread, though there is no acute poisoning. The Thyroxin molecule is structurally similar to Dioxin and competitively inhibits the Thyroxin molecule creating goiters, autoimmune thyroiditis and thyroid cancer.
P7: Genetic analysis of the FMR1 gene for fragile X phenotypes among children attending the Mental Health Clinic at Lady Ridgeway Hospital

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Introduction: Fragile X syndrome (FXS) the known cause of intellectual disability is due to the expansion of CGG repeats in the 5' untranslated region of the Fragile X mental retardation 1 (FMR1) gene. Currently in the Lady Ridgeway Hospital, routine FXS diagnosis is carried out only on records of clinic based assessment. Therefore the present study was aimed at establishing a genetic diagnosis by detecting the CGG repeat expansion of clinically positive FXS children.

Methodology: Seventeen clinically diagnosed FXS individuals (aged 5-12 years) were selected for this study from mental health clinic at the Lady Ridgeway Hospital. Clinic based assessment was made for the presence of phenotypic features compatible with FXS (ICD 10/DSM IV criteria) using cognitive profiles and associated behaviour disorders (Child Behavior Check List). CGG repeat expansions were identified by conventional polymerase chain reaction (PCR) and melt curve analysis (MCA) of the 3’ direct triplet primed PCR (3’dTP-PCR).

Results: Conventional PCR and MCA of 3’dTP-PCR discriminated normal from premutations and full mutations. Among the 17, only a single individual was identified as having expanded repeats from the genetic analysis.

Discussion: According to our results, a frequency of 5.9% clinically diagnosed FXS individuals were positive for the CGG repeat expansion. Therefore it is important to focus on genetic analysis in addition to clinical assessment in diagnosing FXS. However early clinical screening would allow intervention and better quality of life of FXS individuals.

P8: A paternally inherited unbalanced Chromosomal (8;11) Translocation in a Child Presenting with Dysmorphic Features and Seizures

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Reciprocal chromosomal translocations represent one of the most common structural rearrangements observed in humans. We describe a one year old child with dysmorphic features including microcephaly, hypertelorism, upward slanting eyes, epicanthic folds, flat nasal bridge, low set ears, short neck and overlapping toes. The proband was the first child of third degree consanguineous parents born by normal vaginal delivery. He was hypotonic with mild developmental regression and had two episodes of seizures at 8 months and 1 year of age respectively. The other laboratory findings: complete blood count, serum electrolytes, ultrasound scan of the brain and EEG were normal. The initial cytogenetic studies performed on the cultured blood cells by GTG-banding showed translocation between chromosomes 8 and 11; 46,XY,t(8;11)(q24.3;p13). Further investigations were carried out with parental screening. A balanced translocation between chromosomes 8 and 11 was found in the father while the mother had a normal karyotype. Therefore the child’s unbalanced translocation was paternally inherited. The father had a balanced translocation with a normal phenotype but the child had dysmorphism and other features which indicate that the child has an unbalanced translocation with extra or missing genetic material which has been inherited due to malsegregation during meiosis. There is a high chance of an unbalanced translocation occurring in future pregnancies. Break point analysis would give a better understanding of the disrupted genes that are responsible for the phenotype of the child. This may be useful for the treatment and management of the child in the future.
P9: Do we need genetics in Craniofacial Surgery?

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Introduction: Many craniofacial conditions are inherited. Few of studies are available to determine the exact cause of these conditions. However there are several geographic variations reported in the literature. Latest case series have identified a change in the pattern of these conditions. This study focuses on children with craniosynostosis to determine the need for genetic work up to improve parent counseling. So far we are yet to have any publish data for Sri Lanka.

Methods: Patients registered at the craniofacial clinic were employed for this descriptive cross sectional analysis. Data was collected on clinical diagnosis, consanguinity, family history and surgical management.

Results: Of the total 16 patients included in the study isolated sagittal, biconoral, unicoronal, lamboid, multi suture and metopic synostosis were seen in 3 (18.75%), 5 (31.25%), 3 (18.75%), 1 (6.25%), 3 (18.75%), 1 (6.25%) patients respectively. All 5 patients with bicornoral synostosis and 1 of the 3 patients with metopic synostosis showed syndromic features. None of the patients had a significant family history of similar anomalies. Consanguinity was seen only in the single patient with metopic synostosis. Surgical correction was performed in 8 of the 16 (50%) patients.

Discussion: This study shows that all the biconorals and most of multisuture craniosynostosis are syndromic. These children need to be analysed properly to determine the genetic aetiology.

P10: Two siblings presenting with dysmorphism, developmental delay and intellectual disability due to partial trisomy 8p and partial monosomy 18p resulting from a maternal balanced translocation t(8;18)(p21.3;p11.23)

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Numerous structural chromosomal abnormalities have been implicated in the aetiology of dysmorphism, developmental delay and intellectual disability. The underlying chromosomal aberrations can arise either de novo during paternal or maternal meiosis or from unbalanced chromosome rearrangements inherited from a parent with a balanced translocation. A family with two siblings with partial trisomy 8p and partial monosomy 18p resulting from a maternal balanced translocation is described. A 12 weeks spontaneous abortion and death of a male child 9 days after birth due to congenital heart defect were also recorded. The probands were a 9 year old Sri Lankan male child and his 15 years old sister who were referred for cytogenetic evaluation of dysmorphism, global developmental delay, growth retardation and severe intellectual disability. Both siblings had facial dysmorphic features which included large protruding ears, prominent forehead with frontal bossing, hypertelorism and carp mouth. Conventional karyotyping of the children and parents were performed on routinely cultured peripheral blood lymphocytes. All the metaphases from the 2 siblings showed a derivative chromosome 18 with terminal duplication of the short arm of chromosome 8 distal to band p21.3 and partial deletion of the short arm of chromosome 18 at band p11.23. Their mother was a balanced translocation carrier between chromosomes 8 and 18 having the karyotype of 46,XX,t(8;18)(p21.3;p11.23). The probands’ karyotypes were 46,XY,der(18)t(8;18)(p21.3;p11.23)mat and 46,XX,der(18)t(8;18)(p21.3;p11.23)mat. The phenotypic features observed in these two siblings are in keeping with the phenotypes observed in other partial trisomy 8p and partial
monosomy 18p patients reported in the scientific literature.

P11: A maternally inherited partial trisomy 1(q44qter) and partial trisomy 15(pterq22) in a child with Silver Russell phenotype

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The inheritance of a derivative unbalanced chromosome creates a partial trisomy or partial monosomy creating an unbalanced genotype that results in phenotypic features. We report a 1½ year old male baby, the only living child of non consanguineous parents with a history of a previous first trimester miscarriage. The baby presented with feeding difficulty, developmental delay and dysmorphic features including large head, triangular face, high nasal bridge, low set ears with a simple and malformed left ear, long philtrum, bilateral single Palmer creases, bilateral syndactyly and Atrial Septum Defect. Chromosomal culture and karyotyping showed a marker chromosome resulting in an unbalanced structural abnormality. Further analysis by parental screening showed a balanced translocation between chromosome 1 and 15 in the mother; 46,XX,t(1;15)(q44;q22). Therefore the marker chromosome that was present in the child was the derivative chromosome 15 inherited from the mother and the child was carrying partial trisomy of chromosome 1(q44→qter) and a partial trisomy of chromosome 15(p22→pter); 47,XY,+der(15)(t(1;15)(q44;q22). The features of the child correlate with the Silver Russell phenotype that was described in a Dutch family with a de novo duplication while our report is of maternal inheritance. According to our knowledge this is the first report of a patient with maternally inherited 1q duplication showing Silver Russell phenotype. The partial trisomy of 15 q22→pter region has not been previously described. Trisomy 15q24→qter was reported in previous cases as a very rare syndrome and some of the features of our proband overlaps with the features in 15q duplication syndrome.

P12: A baby with a de novo derivative Chromosome 5

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Genomic and chromosomal imbalances are major causes of congenital and developmental abnormalities. Rearrangements in the subtelomeric region of chromosome 5p are commonly seen in patients with Cri-Du-Chat Syndrome. In this case report we describe a baby with a derivative chromosome 5 which has an unknown origin. The baby presented with dysmorphic features – prominent occiput, coloboma, low set small ears, micrognathia, hypospadias, Club foot (surgically corrected) and bulbous nose. The common feature in chromosome 5p terminal derivatives, a cat-like cry was not identified. Cardiac malformations such as Ostium Secundum, Atrial Septum Defect and Patent Ductus Arteriosus were seen. Cytogenetic analysis of the proband showed 46,XY,der(5)add(5)(p15.3). The extra chromosome material could not be specified with cytogenetic studies. Further analysis with parental karyotypes confirmed that it is a de novo rearrangement. Therefore the risk of recurrence is low. When one compare the features and the chromosome rearrangement observed in this baby with that of others reported in scientific literature the phenotype seen here was comparable to classical duplication 5p or Trisomy 5. Increased susceptibility to repeated respiratory tract infections and seizures were also seen in our case which correlates with the phenotype of 5p duplication. Therefore, it is possible that this derivative could be a duplication 5p/ trisomy 5 due to the overlapping of the common features. Further analysis with Spectral Karyotyping with Florescent in Situ Hybridization (SKY-FISH) and Array Comparative Genomic Hybridization (aCGH) is required to identify the origin of this extra material and to confirm the diagnosis.
P13: Phenotypic spectrum of Sri Lankan females with Isochromosome X

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An isochromosome is a chromosome consisting of either two short or two long arms derived by abnormal centromere division or sister chromatid exchange. Isochromosome X is the commonest isochromosome found in humans. Ten to fifteen percent of Turner Syndrome (TS) is due to duplication of the long arm of one X chromosome [46,X,i(Xq)] and some TS patients with mosaicism also have a cell line with isochromosome X. Hypothyroidism is a common association in TS patients with isochromosome X while congenital heart diseases (CHD) are less common than TS patients with 45,X.

We describe a series of 18 female patients with isochromosome X diagnosed at the Human Genetics Unit, Faculty of Medicine, Colombo. Ten patients were referred with suspected TS, six were under investigation for primary amenorrhoea, one had secondary amenorrhoea and another had irregular menstruation. Nine of them had 46,X,i(X)(q10) karyotype, two had 46,X,i(X)(p10), four had 45,X/46,X,i(X)(q10), two had 46,X,i(X)(q10)/46,XX and one had 46,X,i(X)(p10)/45,X. Fourteen patients (77%) had documented gonadal dysgenesis and all of them had either primary or secondary amenorrhoea. All except one had short stature (94%), ten (55%) had cubitus valgus deformity, six patients (33%) had broad chest and eight (44%) had either short neck, webbed neck or both. One patient with isochromosome Xp which is not generally associated with TS phenotype had most of the TS features while one patient mosaic for 45,X/46,X,i(X)(q10) did not have many TS features. In our cohort only four (22%) patients were hypothyroid and none of them had CHD. This study shows the wide variability in the phenotype associated with isochromosome X.

P14: Clinical and genetic characterization of Androgen Receptor (AR) gene mutations in a cohort of Sri Lankan patients with 46,XY Disorders of Sex Development

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Introduction: Androgen receptor (AR) gene plays an important role in male sexual development. Defects in the AR gene result in impaired embryonic sex differentiation in 46,XY genotypic males resulting in Androgen Insensitivity Syndrome (AIS). This study aims to describe the clinical and genetic characteristics of AR gene mutations in a Sri Lankan cohort with 46,XY disorders of sex development (46,XY DSD).

Methods: The AR gene was tested for mutations by sequencing the gene in 45 karyotypically confirmed Sri Lankan patients with 46,XY DSD.

Results: Pathogenic missense mutations located in exons 3, 4, 6 and 7 of the AR gene were identified in 12 (26.7%) patients. Complete androgen insensitivity syndrome (CAIS) phenotype was observed in 9 (20.0%) phenotypic females presenting with inguinal masses and/or primary amenorrhoea. The partial phenotype (PAIS) was seen in 3 (6.7%) undervirilized males who presented with ambiguous genitalia. A novel missense mutation causing a hemizygous nucleotide substitution in exon 6 was identified (NM_000044.3 (AR): c.2326 A>G; p.M776V). This change causes a non-synonymous substitution in the ligand binding domain within the AR protein which is predicted to be deleterious. The modified function of the predicted AR protein is considered to be responsible for the CAIS phenotype observed in this patient. The remaining pathogenic mutations have been documented in literature.

Discussion: AR gene mutations play an important role in the aetiology of 46,XY DSD in Sri Lankans. CAIS should be considered in phenotypic females presenting with inguinal masses/primary amenorrhoea and PAIS in undervirilized males with ambiguous genitalia.
P15: A Child with a novel de novo mutation in the Aristaless Domain of the Aristaless-Related Homeobox (ARX) gene presenting with ambiguous genitalia

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Introduction: Many gene mutations are associated with disorders of sex development (DSD) and hence the whole exome sequencing approach represents a relatively rapid and cost effective diagnostic technique to understand the aetiology. The objective of this study was to identify novel disease-causing mutations in a patient with 46,XY DSD using this approach.

Methods: Whole exome sequencing was performed on DNA from blood samples of a 3.5 year old Sri Lankan male child presenting with ambiguous genitalia. The Illumina HiSeq2000 platform was used and novel variants were analyzed by a range of web-based bioinformatics tools.

Results: The patient had a 46,XY karyotype with under-virilized male genitalia. A novel mutation in the aristaless-related homeobox (ARX) gene causing a hemizygous nucleotide substitution in exon 5 was identified (NM_139058.2 (ARX): c.1614G>T; p.K538N). This change causes a non-synonymous substitution in the C-terminal aristaless domain within the ARX protein which is predicted to be deleterious. The modified function of the predicted ARX protein is considered to be responsible for the phenotype observed in the proband. This mutation was not present in either parent and is de novo.

Discussion: This is the first reported case of abnormal genital development associated with a missense mutation in the aristaless domain within the ARX protein. It highlights the importance of exome sequencing even in sporadic cases of DSD. This case adds to the spectrum of genetic variations seen in patients with 46,XY DSD. It is suggested that ARX screening should be considered in genotypic males with abnormal genital development.

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P16: Maternally inherited unbalanced chromosomal (1;17) translocation presenting with craniofacial dysmorphism, developmental delay, and multiple congenital malformations

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Although many syndromes resulting from chromosomal rearrangements are described in scientific literature, a dysmorphic phenotype resulting from chromosome (1;17) translocation has not been reported. We report the first case of maternally inherited unbalanced chromosome (1;17) translocation presenting as craniofacial dysmorphism, developmental delay, and congenital malformations.

A five months old Sri Lankan male child was referred to the genetic clinic due to facial dysmorphism and global developmental delay associated with cardiac and renal malformations. On examination the baby had microcephaly, asymmetrical face, frontal bossing and bitemporal narrowing, large low set posteriorly rotated ears, hypertelorism, upward slanting eyes with long eye lashes, prominent eye brows, flattened nasal bridge, bulbous nasal tip, smooth philtrum, abnormal hairline, cryptorchidism and a sacral dimple. The fifth fingers showed clinodactyly and the third toe was overlapping the second toe in this child with generalized hypotonia. 2-D echocardiography confirmed atrial septal defect, ventricular septal defect and patent ductus arteriosus. Investigations showed dysplastic kidneys and two cysts in the brain. Cytogenetic analysis identified a balanced chromosomal translocation 46,XX,t(1;17)(p36.3;q22) in the mother and an unbalanced chromosomal rearrangement, 46,XY,der(1)t(1;17)(p36.3;q22)mat in the child. The child has inherited a derivative chromosome 1 with partial deletion of 1(p36.3pter) and partial trisomy of chromosome 17(q22qter). This finding broadens the knowledge on clinical phenotypes caused by chromosomal rearrangements. Furthermore this emphasizes the importance of genetic counseling and karyotyping of parents to
detect phenotypically normal balanced translocation carriers in order to prevent recurrence.

P17: Child with maternally inherited pericentric inversion of chromosome 9 presenting with dysmorphism, developmental delay and multiple congenital malformations

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Although inversion of chromosome 9 causing subfertility and miscarriages are well described in scientific literature, little is known about the phenotypes caused by chromosome 9 inversion in dysmorphic children. We report a dysmorphic baby with developmental delay and multiple congenital malformations resulting from a maternally inherited pericentric inversion of chromosome 9.

A six months old Sri Lankan female child was referred to the genetic clinic due to facial dysmorphism and global developmental delay associated with cardiac and limb abnormalities. On examination the baby had microcephaly, low set ears, partial ptosis, downward slanting eyes, epicanthal folds, down curved mouth, micrognathia and a short neck. Her left second and third fingers and right third finger showed congenital deformities. Her feet showed plantar cleft. Shone’s anomaly (supravalvular mitral membrane, valvar mitral stenosis by a parachute mitral valve, subaortic stenosis, and aortic coarctation) was confirmed by 2D echocardiography.

Cytogenetic studies revealed pericentric inversion in the region p13-q13 in chromosome 9 \([46,XX,inv(9)(p13q13)]\) in the proband. Maternal karyotype \([46,XX, inv(9)(p13q13)]\) showed the same pericentric inversion revealing a phenotypically normal carrier. Paternal karyotype was normal. Therefore cytogenetic studies concluded that this baby’s chromosomal rearrangement was maternally inherited \([46,XX, inv(9)(p13q13)]\). This finding broadens scientific knowledge on the clinical phenotypes caused by chromosomal rearrangements and emphasizes the importance of genetic counseling and karyotyping of parents to prevent recurrence. Further studies are needed to explore the genetic, epigenetic and environmental causes which contribute to different phenotypical expressions of genetic variants through generations.

P18: A rare case of Type1 Spinal Muscular Atrophy in non-identical twins following \textit{in-vitro} fertilization

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Spinal muscular atrophy (SMA) is characterized by progressive degeneration of alpha motor neurons in the spinal cord, caused by homozygous mutations in the survival motor neuron 1 (SMN1) gene. Identical twins affected with SMA is not unusual but we report a rare case of homozygous disease in non-identical twins conceived following \textit{in-vitro} fertilization.

Five months old, non-identical twins (of opposite sex) were referred to the Teaching Hospital Peradeniya for chronic cough. Parents were distantly related and underwent \textit{in-vitro} fertilization (in India) for primary subfertility of 10 years duration. Birth and early infancy were uneventful. Parents noted absence in achieving head control in both infants but they interacted well with social smile, startle response and age appropriate vocalization. On examination, apart from symptoms of a respiratory tract infection, it was noted that both exhibited minimal limb movements with hypotonic posture, absent deep tendon reflexes and tongue fasciculations. Facial muscles were unaffected. SMA was suspected and electromyography (EMG) revealed anterior horn cell disease pattern. Molecular genetic studies confirmed the diagnosis demonstrating homozygous deletions of exon 7 and 8 in \textit{SMN1} gene. The parents were not interested in carrier testing. Both twins died subsequently due to progressive respiratory insufficiency.

Many centers performing \textit{in-vitro} fertilization in less developed nations still experience a high failure rate as well as unfavorable outcomes depicted by the above case. Pre-implantation genetic screening (PGS) technology can be a solution for both problems. SMA is one of the many diseases which can be effectively diagnosed using PGS.
P19: A case series of four Sri Lankan patients with 5p deletion

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Cri-Du-Chat syndrome, also known as 5p-syndrome is one of the most common human deletion syndromes, which results from deletion of varying lengths of the short arm of chromosome 5. The characteristic feature is neonates presenting with high pitched cat like cry, considered to be clinically confirmatory of the syndrome.

We describe four Sri Lankan patients with 5p-syndrome. Three of them had the de novo deletion of 5p. Their karyotypes were 46,XX,del(5)(p13), 46,XX,del(5)(p14→15.3) and 46,XX,del(5)(p14) respectively. They depicted most of the features of Cri-Du-Chat syndrome, such as round face, microcephaly, hypertelorism, downward slanting palpebral fissures, epicanthic folds, large nasal bridge, low set ears, micrognathia, down turned corners of the mouth and bilateral simian creases.

The other patient carried a derivative chromosome which resulted from a paternal transmission of a balance translocation. Her Karyotype was 46,XX,der(5)add(8)(q13)del(5)(p13)pat. Her father’s Karyotype was 46,XY,t(5;8)(p13;q13). This is the first case reported to be having a monosomy 5p and a trisomy 8q. Her clinical features overlapped with both 5p deletion and trisomy 8q syndromes. She had some characteristic features of Cri-Du-Chat syndrome such as large nasal bridge, hypertelorism, low set ears and micrognathia and some features characteristic of trisomy 8, such as long slender body, full everted lower lip, wide apart nipples and septal defects of the heart. She also had upward slanting eyes with a divergent squint which was not reported in either syndrome before.

P20: Karyotype-phenotype correlation in partial monosomy of the long arm of chromosome 13: A case report

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The 13q-syndrome is characterized by structural and functional monosomy of the long arm of chromosome 13. The wide spectrum of phenotypes associated with this condition varies between chromosome 13q deletions depending on the location and the size of the deleted region. This syndrome is classified into three groups with regard to the band 13q32. Group 1 consists of deletions proximal to q32, group 2 includes q32 and group 3 has deletions in q33-34. Irrespective of the groups, the most common clinical features seen in this condition are mental and growth retardation, craniofacial dysmorphisms, hand and foot anomalies, and brain, heart and kidney defects. A dysmorphic 2 years and 9 months old girl with short stature, microcephaly, partial ptosis with a divergent squint and hazy iris, low set ears, broad nasal root with shallow bridge, micrognathia, short philtrum, open mouth with thin lips and cleft palate, clinodactyly, brachydactyly, citoromegalgy and overridden second toe was subjected to cytogenetic testing. She also had repetitive movements with poor focus and global developmental delay. The cytogenetic test revealed a 46,XX, del (13)(q31qter) abnormal karyotype. A possible correlation between the deleted region and the distinctive features was reported in the literature. The critical region is located at 13q32, which is implicated with severe phenotypes. Molecular characterization of the deleted region should be done in an attempt to address the genes disrupted.
P21: A Male Infant with Partial Monosomy of 7p21 Syndrome Associated with Craniosynostosis, Craniofacial Dysmorphism and Non Communicating Hydrocephalus

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A two weeks old male infant with dysmorphic features was referred to the Human Genetics Unit for genetic diagnosis. The clinical features of the child included craniosynostosis and facial dysmorphisms such as hypertelorism, bilateral epicanthal folds with short upward slanting palpebral fissures, ptosis, flat nasal bridge, a long smooth philtrum, mild micrognathia and tented upper lip. He had prominent helical crura and transverse creases of hands bilaterally however there was no evidence of soft tissue syndactyly. Ultrasound scan of the brain revealed ventriculomegaly and 2D echocardiogram showed evidence of congenital heart disease: Patent Ductus Arteriosus and Atrial Septal Defect. An abdominal ultrasound scan was normal. There was no family history of similarly affected individuals. Karyotyping revealed a de novo terminal deletion of the short arm of chromosome 7 (46 XY,del(7)(p21pter). Among the developmental regulator genes found in this region TWIST 1 is the gene mostly matched with the infant phenotype. TWIST1 gene is located in 7p21 region and haploinsufficiency is associated with craniosynostosis. Micro deletion of chromosome 7p21.1 region is responsible for four types of syndromes: Craniosynostosis type 1, Robinow Sorauf syndrome, Saethre-chotzen syndrome and Saethre-chotzen syndrome with eye lid anomalies. For further genotype phenotype correlation of this child targeted molecular genetic testing is required.

P22: Chromosomal aetiology of 669 cases of syndromic and non-syndromic birth defects: A summary report


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Abnormalities in structure, function or metabolism which are present at birth are called birth defects or congenital anomalies according to the World Health Organization (WHO). Global incidence of birth defects is 1 in 33 in infants and it has contributed to the fourth largest reason for neonatal deaths in 2012 in 193 countries. Genetic abnormalities play a major role in the aetiology of birth defects. We summarize chromosomal aetiology of 669 syndromic and non-syndromic birth defects cases from 2006 to 2013 referred to a genetic clinic. Out of 2,419 cases referred, we excluded cases of recurrent miscarriages, subfertility, and cases of dysmorphic features reported with normal karyotypes. Out of selected 669 cases, 52.9% were female and 47.1% were male. Numerical chromosomal abnormalities accounted for 89.9% including the syndromic phenotypes such as Down syndrome, Turner syndrome, Klinefelter Syndrome, Patau syndrome and Edward syndrome, with an exception of 49,XXXY case. Structural abnormalities such as isochromosomes (3.7%), deletions (1.4%), robertsonian translocations (2.7%), inversions (0.4%), ring chromosomes (0.7%), marker chromosomes (0.6%) and derivative chromosomes or reciprocal translocations (0.6%) accounted for 10.1%. The most affected chromosome in structural abnormalities was the chromosome X due to isochromosomes and partial deletions detected in cases of Turner syndrome and primary amenorrhoea. Chromosomes 21 and 14 contribute to the second and third places due to robertsonian translocations manifesting as Down syndrome. Chromosomes 4, 9, 15, 1, 18, 8, 11, 5, 7, 6 had contributed to the other structural chromosomal abnormalities manifesting with various birth defects.
P23: Phenotype of partial trisomy of chromosome 8(p21→pter) and partial monosomy of chromosome 11(q25→qter); A case of dysmorphic features and global developmental delay.


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We report an individual with partial trisomy of chromosome 8(p21→pter) and partial monosomy of chromosome 11(q25→qter). At presentation the child was 2 years old and had distinct dysmorphic features: brachycephaly, low set simple ears, thick eye brows, bilateral partial ptosis, downward slanting palpebral fissures, broad nasal bridge, large carp shaped mouth with thick lip and everted lower lip, microglossia, long philtrum, slender extremities, clinodactyly, hyper pigmented nodules on the trunk, café au-lait spots on trunk and 2 mongolian spots. The child was hypotonic and had a history of global developmental delay. Due to behavioral changes he was suspected to be having autism spectrum disorder. Cytogenetic analysis of peripheral blood lymphocytes showed a derivative chromosome 11 with extra chromosomal material. Parental karyotyping showed a balanced translocation in the father involving chromosome 8(p21→pter) and chromosome 11(q25→qter), resulting in a derivative chromosome 11. The karyotype of the child was 46,XY,der(11)t(8;11)(p21;p25)pat

The same chromosome abnormality with same breakpoints of maternal origin has been described once before in scientific literature. Hence we describe the second case with the same breakpoints, but of paternal origin. Comparison between the phenotypes of the child reported by us and the individual described before revealed that they have both overlapping and non-overlapping features. This could be explained by differences in the genes involved in the exact chromosomal breakpoints or by differences in genetic imprinting.

P24: Descriptive study of genetic services provided at De Soysa Hospital for Women from September 2012 to December 2013

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Introduction: Genetics is playing a central role in provision of Obstetrics and Gynaecology care. The first clinical genetics service in a Women’s Hospital in Sri Lanka was set up at the De Soysa Hospital for Women (DSHW) in September 2012. The objective of this paper is to describe the clinical genetics services provided at DSHW.

Methodology: A detailed case record, including the family history, was maintained for each and every family referred for genetic consultation. These records were analysed retrospectively for the period September 2012 to December 2013.

Results: A total of 215 families were referred. The indications were 82(38.14%) maternal, 54(25.11%) gynaecological, and 79(37.75%) paediatric. The maternal referrals were: known single gene defect 14(6.51%), bad obstetric history 24(11.16%), prenatal detection of birth defects 40(18.6%), others 4(1.86%). The gynaecological referrals were: recurrent miscarriages 31(14.42%), primary amenorrhoea 8(3.72%), primary subfertility 5(2.32%), others 10(4.65%). The paediatric referrals were: syndromic children 31(14.42%), babies with multiple congenital anomalies 41(19.06%), and multifactorial diseases 7 (3.25%). The number of patients where genetic testing was indicated and testing was performed was as follows – Maternal: Indicated - 58(70%); performed – 17(20%); Gynaecological: Indicated – 51 (94%); performed – 14(25%); Paediatric: Indicated – 72 (91%), performed – 20 (25%).

Conclusions: This report for the first time in Sri Lanka documents the Clinical Genetics workload in a Women’s Hospital. A significant proportion of patients for whom genetic testing was indicated could not be tested because they could not afford genetic testing. Therefore it is necessary to set up a scheme for the Ministry of Health to finance genetic testing.
P25: A ring chromosome 21 in a child with dysmorphic features


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Ring chromosome 21 is a rare chromosomal aberration associated with recognizable dysmorphic features, malformations and mental retardation. Deletion of genetic material of both ends of the chromosome in ring formation is responsible for the manifested phenotypes. In addition secondary loss or gain of genetic material can occur due to the instability of ring chromosome via formation of dicentric rings and isochromosomes. This case describes dysmorphic features of a six months old male baby with ring chromosome 21 who was tested by routing cytogenetic analysis. The karyotype of the baby was 46,XY,r(21). One of the normal homologues of chromosome 21 was replaced with ring configured chromosome 21 in every analyzed spread. The manifested phenotypes included flat occiput, mildly low set ears, upward slanting eyes, epicanthal folds and flat nasal bridge suggestive of Down syndrome. Ring chromosome 21 detected in the patient was concluded as de novo after his mother and father were found to have normal karyotypes. Parents were given genetic counseling. Further studies are arranged to characterize the genomic structure of the ring chromosome using molecular-cytogenetic techniques, as it is important to correlate the phenotypes of the individual with the loss or gained genetic material in the r(21) formation mechanism.

P26: De novo segmental duplication of 15q, confirmed by chromosomal microarray and FISH, in a child with global developmental delay and facial dysmorphism

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Segmental duplication or partial trisomy of chromosome 15q, is an extremely rare chromosomal disorder characterized by mental retardation and craniofacial malformations. The range and severity of the symptoms and physical findings may vary from case to case, depending upon the length and location of the duplicated portion on the chromosome 15q. Besides prenatal and postnatal overgrowth, additional abnormalities may include a short neck, malformations of the fingers and toes, scoliosis and skeletal malformations, genital abnormalities, and in some cases, cardiac defects. Most reported cases of duplication of the long arm of chromosome 15 frequently have more than one segmental imbalance resulting from unbalanced translocations involving chromosome 15 and deletions in another chromosome, as well as other structural chromosomal abnormalities.

We report a four year old male child with global developmental delay and behaviour problems along with facial dysmorphisms thus warranting a cytogenetic work-up. The array comparative genomic hybridization analysis revealed a duplication of 15.1Mb at cytoband 15q21.2q22.31 containing several genes. This duplication was further confirmed by FISH. This case represents a patient with a de novo 15q segmental duplication that did not result from an unbalanced translocation and did not have a concomitant monosomic component in any other chromosome.
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