Dr Cyril Fernando Memorial Oration 2009

Multifaceted manifestations of paediatric endocrinology

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I wish to thank most sincerely the President and the members of the Council of the Ceylon College of Physicians (CPP) for awarding me the Cyril Fernando Memorial Oration for 2009. It is indeed a great honour.

Dr Cyril Fernando was born on the 30th of April 1900 in Colombo. He was educated at St. Benedict's College and University College Hospital, London. He obtained the MBBS in 1926 as well as the MRCP. On his return to Ceylon he joined the Colonial Medical Service and served as a Medical Registrar at the General Hospital, Colombo. In 1929 he obtained the MD in UK and for his outstanding performance he had been exempted from an essential component of that examination. He was also awarded the gold medal for the best candidate of that year.

Returning to Ceylon he held several posts such as Assistant Pathologist, GHC, Physician / OPD and in 1934, Visiting Physician to the GHC which post he held until his demise. He had been an active member of the Ceylon branch of the British Medical Association and held the posts of Honorary Secretary, Treasurer and Vice President of the Ceylon Medical Association and in 1948 he was elected President of the Association. For his services to medicine in Ceylon he was twice honoured by the Sovereign. In 1949 he was appointed an Officer of the Most Excellent Order of the British Empire and in 1955 he was made a companion of the Most Distinguished Order of St. Michael and St. George.

For obvious reasons I did not know him. But he had been an excellent clinician and diagnostician, blessed with the healing touch, a fantastic teacher with a great sense of humour and a good friend. Loved and respected by his colleagues and patients, this great physician passed away in November 1955 while still serving his country.

I am truly honoured and privileged to deliver this oration today in the memory of such a great son of our country and I am very grateful to the President and the Council of the CCP for giving me this opportunity.

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Introduction

Hormones play an important role in the life sequence of a child from differentiation of sex in-utero to growth and development up to puberty and adolescence. During this period of time, the constantly changing demands of the external and internal environments are met by the endocrine system modifying the activities of the various body mechanisms to maintain normalcy within the human body. This process of integration is brought about by hormones which are chemical messengers produced by ductless glands and transported in the circulation to target cells. The complex system of stimulation, inhibition and feedback control of hormone secretion regulates the biological effects of these chemicals within defined physiological limits maintaining homeostasis of the milieu interior.

Genes and endocrinology

Endocrinology and molecular biology are closely linked. A sound understanding of molecular biology and the rapid advances in technology combine to provide the necessary answers regarding causation of disease associated with endocrine organs. Genes encode production of each of these chemicals and the receptors which are essential for the action of these hormones. Mutations / deletions of one or more of these genes and also tumours, cause either hyper or hypo secretion of these essential hormones with long lasting effects on the child.

We in Sri Lanka do not have the facilities to diagnose most of these disorders at molecular level. But we can clinically identify, investigate and treat these conditions within the constraints of working in a developing country. Following is an account of a journey spanning 8 years, detailing studies that were done and presently ongoing, problems faced and lessons learnt, in caring for children affected by the endocrine cascade.

The journey begins…

Effect of hormones in fetal life

The fervent wish of every parent is for their baby to be born normal and healthy. But sometimes things go horribly wrong and babies are born with ambiguous genitalia when it is extremely difficult to identify the sex of the baby at birth. 1 in 4500 births world wide

will result in such a baby being born. These conditions are collectively known as disorders of sex development (DSDs)[1].

A myriad of causes which can be explained on a genetic basis, from sex chromosome abnormalities, absent or inadequate production of testosterone due to dysgenetic gonads or partial or total lack of action of testosterone due to insensitivity at receptor level or deficiency of enzymes in the biosynthetic pathway of production of the male hormone result in under-virilization of a male fetus and the baby boy being born with ambiguous genitalia[2,3].

When the degree of ambiguity is severe irrespective of the karyotype, the extremely important decision as to the sex of rearing has to be made. When dealing with this very sensitive issue, views of the family and cultural practices are of paramount importance in our country[4,5] and the parents make this important informed decision according to what they think is the best option for their child. This story illustrates the importance of making an informed decision as early as possible and therefore probably by the parents, contrary to views expressed by patient advocacy groups[3,6].

Case history

A baby was born in 1989 in a little village in the Sabaragamuwa Province of Sri Lanka. She was referred to us at the age of 12 years because she was insisting that she be 'turned into a boy'. She was the second child of unrelated parents who had always preferred the company of boys. On presentation to Lady Ridgeway Hospital (LRH) examination of the systems was normal. There was a 2.5cm phallus with bifid scrotolabial folds, bilateral 3ml palpable gonads with a perineal urethra. Her mother had always thought that this appearance was abnormal and had shown the child several times but had only been reassured! Investigations confirmed that she was indeed a boy. Ultrasound scan of the abdomen identified a rudimentary uterus confirming the diagnosis of 46, XY partial gonadal dysgenesis. She was treated with testosterone and had reconstructive surgery. Their troubles did not end there. They had to change their residence and he had to change his school. They encountered problems changing his birth certificate. They received psychological support through this very trying period of their lives. He is almost 20 years now and continues to have certain issues which are being dealt with by the adult endocrinologist.

Complete androgen insensitivity (CAIS) is when testosterone is produced by the normally functioning testes but there is total insensitivity to its action at receptor level. The baby then has completely normal female external genitalia and would present later with primary amenorrhoea or inguinal herniae containing the prolapsed testes.

We have two such children where the parents made informed decisions regarding their future. One child presented at 5 months of age with lumps in the labia which were subsequently identified as testes. After several sessions of counselling the parents opted against removal of the gonads till the child was older. The other girl was referred by the surgeons with bilateral inguinal herniae containing gonads which her parents wanted removed. Both girls will be seen at the appropriate age for reconstructive surgery and hormone replacement therapy.

Role of adrenal steroids in 'mistaken identity' – Masquerade! (unintentional)

Adrenal glands are small but remarkable and essential for life. Similar to all other endocrine glands, excess, diminished or absent production of several hormones secreted by these glands cause diseases which are rare in children. The adrenal cortex produces cortisol which is essential for life, aldosterone without which the salt and water balance of the body cannot be maintained and androgens which are secreted in both boys and girls. These steroid hormones which are derivatives of cholesterol are produced in the 3 zones of the cortex, each step in the 'production pathway' being dependant on the action of various enzymes. Each of these enzymes are encoded by genes, mutations of which cause deficiency of these chemicals interrupting different steps of the adrenal steroid pathways, resulting in absence of some hormones and overproduction of others with accumulation of precursors.

Autosomal recessively inherited congenital adrenal hyperplasia (CAH) is the commonest adrenal disorder affecting children[2] with a worldwide incidence of 1:12000. Deficiency of the enzyme 21 hydroxylase (21OH) due to a gene mutation expressed in 2 zones of the cortex results in absence of cortisol and aldosterone and over production of androgens. This process occurs in fetal life and an affected baby girl is born with ambiguous genitalia due to excess androgens. In the absence of cortisol, ACTH increases causing progressive pigmentation of the baby. This condition is fatal unless they receive adequate replacement therapy. With the institution of appropriate treatment the previously pigmented, emaciated babies begin to thrive and get back the complexion they were destined to have.

When 21OH deficiency is expressed only in one zone, there is no dehydration and the lack of cortisol may not be severe enough to cause symptoms necessitating admission to hospital. The affected baby

girls may present early with ambiguous genitalia or later with virilization manifesting as hirsutism, tall stature and genital changes. When undiagnosed and untreated they maybe brought up as boys. We have two such children and mere words cannot describe the psychosocial turmoil that these children and their parents had to endure and will continue to do so for a long time to come. These stories highlight the importance of all medical personnel caring for children being aware of these rare conditions so that they can be detected early and treated appropriately.

Case history

A little boy, 6 years and 2 months of age, was transferred from the Eastern Province in 2002[7]. He was the first born of a consanguineous union. He had been a healthy boy growing and developing normally with no hospital admissions. Since 3 years of age he had gradually become hoarse and had evidence of virilization with appearance of pubic hair, phallic enlargement and facial acne. Rapid progression of these features over about 6 months prompted the parents to seek medical advice.

He was dark and very tall. Examination of the systems was normal. Stage III pubic hair was present with empty hyper pigmented, underdeveloped scrotal sacs and a 8.2cm phallus. Investigations revealed that this child was indeed a girl with very high levels of serum 17 hydroxy progesterone and androgens with an advanced bone age. Ultrasound scan examination identified enlarged adrenal glands with female internal organs. This child therefore was a completely virilized girl with undetected and untreated non salt losing 21 hydroxylase deficiency CAH. He was a well adjusted boy with a male gender identity. Following several discussions, the parents decided against a gender reassignment.

This little boy's problems are not over yet. He had to undergo surgery to remove the female internal organs and the family is aware that he will be infertile. Although very tall now he is going to be a short adult. What of his future? Only time will tell…

A four and a half year old boy was sent for evaluation. The product of a cousin marriage, this child had always been dark and very tall, being the tallest in his class at his preschool. He had been investigated and treatment started at 2 years of age but the compliance had been extremely poor. Over the previous year he had developed body hair, pubic hair and acne with phallic enlargement. Examination of the systems was normal with a normal blood pressure. He had a 5cm phallus with a perineal urethra. The fused 'scrotolabial' folds were pigmented and rugose without palpable gonads. Investigations confirmed that this child too was an extremely virilized girl due to inadequately treated CAH. His behaviour and gender identity were male. When the condition with possible future implications was discussed with the parents, they wished for a gender reassignment. Because this decision was probably not in the best interest of the child, we had further discussions with the parents during which they defaulted follow up.

Effect of hormones on the growth of a child

'Different tissues and different regions of the body mature at different rates, and the growth and development of a child consist of a highly complex series of changes. It is like the weaving of a cloth whose pattern never repeats itself, each underlying thread coming off its reel at its own rhythm and interacting with the others continuously, in a manner which is always highly regulated and controlled. The fundamental questions of growth relate to these processes of regulation, to the programme that controls the loom. We understand very little about this so far' - *J. M. Tanner.*

Growth is an integral part of a child's life. Along with thyroxine, growth hormone is essential for this process. This polypeptide is secreted by the anterior pituitary gland of the human brain. Hyper secretion of growth hormone in children is rare. Although the incidence of growth hormone deficiency in Sri Lankan children is not known, there are children scattered throughout the country with absent or minimal production of growth hormone.

Growth hormone deficiency (GHD) occurs due to causes varying from genetic disorders to structural abnormalities. Whatever the underlying cause, the effect on the child is devastating. Majority of these children are otherwise healthy and of normal intelligence and are trapped inside their bodies which cannot grow without treatment and would be extremely short adults as growth hormone (GH) accounts for approximately 38cm of postnatal growth in boys and 33cm in girls.

Since September 2002 we are following up children with confirmed GHD8 referred to us from all over Sri Lanka. There are 35 boys and 10 girls, their ages ranging from 15 years and 3 months to 4 years at diagnosis. GH being very expensive, only 13 parents could purchase it. Treatment was discontinued in 9 after receiving it for periods varying from 5 to 18 months due to lack of funds. The others never got GH. The children on treatment are doing well and gaining centimetres beyond their wildest expectations! Parents are happy with the outcome albeit the enormous expense.

What do these children really feel, living with GHD? We hypothesized that they would have negative psychological ramifications due to its potential impact on their psychological constructs such as self esteem. It was also possible that this condition would have an impact on the parents' psychological health. To study this concept further, we used The Personality Assessment Questionnaire (PAQ) validated to be used with Sri Lankan children, to see whether they were psychologically affected by their condition[9,10]. This self-administered questionnaire was given to children over 8 years of age. This assesses whether a child is psychologically maladjusted and is measured in 7 dimensions: Hostility and Aggression, Dependency, Negative Self-Esteem, Negative Self-Adequacy, Emotional Unresponsiveness, Emotional Instability and Negative World View. Response options are given scores from 1 to 4 in the 42 items and 14 of these are reverse scored to prevent 'blind' answering. A score of ≥ 89 is indicative of psychological maladjustment in the child. There were 32 children over 8 years of age with 26 boys. A significant score on the PAQ was obtained in 22 children (68.8%). Eighteen were boys (81.8%) and eleven were older than 12 years.

Their parents are also affected knowing there is a drug to make their children grow but that it cannot be given as they cannot afford it. We gave the self-administered General Health Questionnaire-30 (GHQ-30:30 items) where each response is given a score to assess the impact on the parents. A score of ≥ 4 identifies the test taker as having mental health difficulties[11]. Fifty two parents, 34 of whom were mothers (65.4%), answered the questionnaire. Twenty two mothers and 8 fathers (30 - 57.7%) had a significant score implying the presence of mental health difficulties in these parents (Table 1). From this limited study where the numbers are small, apart from commenting on the hypotheses which appeared to be valid, causality between GHD and psychological health cannot be established. But it does give an insight to the psychological trauma of living with GHD and the impact on the parents.

Table 1. Psychological assessment of children with GHD and their parents

Personality assessment questionnaire (n = 22) Score ≥ 89

Age (years)	*<12*	*>12*	*Total number*	*Percentage*
Boys	7	11	18	81.8
Girls	3	1	4	18.2

Assessment of parents – General Health Questionnaire-30

	Mothers	*Fathers*	*Total*
GHQ-30	34	18	52
Score ≥ 4	22	8	30 (57.7%)

Since February 2009 all these children are receiving GH from the Lady Ridgeway Hospital free of charge and thus they will be able –

'To dream the impossible dream
To fight the unbeatable foe
To bear with unbearable sorrow
To run where the brave do not go
To right the unrightable wrong
To love pure and chaste from afar
To try when your arms are so weary
To reach the unreachable star' – Cervantes

They will continue to be followed up till treatment is discontinued.

Nutrition and metabolism

'The lot of fat children is a sad one. They are bashful and ashamed of their shapeless figures, yet unable to conceal them. Wherever they go they attract attention… Obesity is a serious handicap in the social life of a child, even more so of a teenager. Obesity does not have the ''dignity'' of other diseases and it is not always taken seriously, even by adults' – *Bruche*

Malnutrition is not an alien issue to Sri Lankan Paediatricians. Under nutrition was the form of malnutrition they have been grappling with for a long time. Since of late, another form of malnutrition has reared its ugly head amongst our children. Obesity is increasing worldwide in epidemic proportions with associated morbidity and mortality due to metabolic syndrome (MetS) and non-alcoholic steato-hepatitis (NASH). MetS leads to atherosclerotic cardiovascular disease and type II diabetes mellitus while NASH can progress to cirrhosis[12,13]. A prevalence of childhood obesity of 4% and overweight of 11% was reported from an urban area of Sri Lanka in 2004[14]. A separate Obesity and Diabetes Clinic was started at LRH in January 2004 as we thought these children needed more focused attention.

Metabolic derangements associated with childhood obesity had not been previously reported in Sri

Lanka. Therefore we studied these children with the intentions of documenting the presence of MetS and NASH and to compare the association of waist circumference (WC) and body mass index (BMI) with the metabolic derangements[15]. We studied 70 obese children (40 boys) over the age of 2 years from November 2004 to September 2005. We defined obesity, MetS, NASH, hypertension and abnormal glucose homeostasis which included impaired glucose tolerance (IGT) and insulin resistance for our study based on a modification of the IDF 2004 guidelines[16]. The findings were startling. Three children were already having type II diabetes mellitus. Sixteen children had evidence of insulin resistance which is expressed as HOMA-IR (homeostasis model assessment-insulin resistance: calculated using fasting insulin and fasting blood glucose). This manifests clinically as acanthosis nigricans, Furthermore, 13 (21%) had MetS and 11 (18%) had NASH. We also found that the different components of MetS (TG, SBP, DBP, HOMA-IR) were more significantly associated with the waist circumference in children than the BMI (Tables 2 - 5). We concluded that the WC and acanthosis nigricans could be used for screening overweight and obese children for early identification of potentially serious metabolic abnormalities.

Table 2. Demographic features of the study population

	Boys mean (SD)	*Girls mean (SD)*
Number	40	30
Age (years)	9.7 (2.5)	9.3 (3.0)
BMI (kg/m^2)	25.9 (3.6)	25.9 (4.4)
WC	84.2 (11.4)	84.0 (12.0)
HC	85.7 (10.9)	90.1 (12.2)
WHR	0.98 (0.05)	0.93 (0.05)
FM (kg)	24.2 (10.1)	26.7 (10.9)
% FM*	47.5 (5.7)	48.6 (10.9)

* % Fat Mass (%FM) associated with adverse health outcomes – >25% in boys and >32% in girls

Table 3. Components of the metabolic syndrome in the study population

	Boys	*Girls*	*%*
WC (> 98th percentile)	40	30	100
TG n=70 (> 95th percentile)	18	9	39
HDL n=70 (<5th percentile)	1	1	3
HBP n=70 (≥95th percentile)			
SBP	5	3	11
DBP	0	3	4
Abnormal glucose homeostasis n=63	9	8	27
Metabolic syndrome n=63	5	8	21

Table 4. Liver involvement in the study population (n=60)

		Boys	*Girls*	*%*
Liver score	1 - 3	18	12	50
	4 - 6	-	-	-
	7 - 9	-	-	-
ALT (> 40 iu/l)*		12	3	25
NASH		9	2	18

* Upper limit of normal for the reference laboratory

Table 5. Association of obesity indicators with metabolic derangements

	TG	*SBP*	*DBP*	*HOMA-IR*
WC	r=0.24 p=0.04	r=0.58 p<0.001	r=0.48 p<0.001	r=0.32 p=0.01
BMI	r=0.22 p=0.07	r=0.41 p<0.001	r=0.28 p=0.02	r=0.21 p=0.09
WHR	r=0.1 p=0.43	r=0.28 p=0.02	r=0.25 p=0.03	r=-0.09 p=0.49

Hormones on the rampage – A raging inferno!

Puberty is the period of final maturation of the gonads with the possibility of reproduction. Although the exact stimulus is not known, sequential changes in endocrine activity is responsible for physical and psychological changes of pubertal development.

No longer a child to run to the safety and comfort of their parents' arms, but older and supposedly wiser, striving to be accepted as an adult but not quite an adult yet, this period of time known as adolescence is a time of great emotional upheaval, even to the most stable child coming from a loving and supportive family environment.

When there is premature activation of the hypothalamo-pituitary-gonadal axis the events of puberty occur at the wrong time: before 8 years in girls and 9 years in boys. This is known as central precocious puberty (CPP) when the pattern of endocrine changes is the same as in normal puberty, and development is consonant. This is almost always due to intracranial pathology in boys but mostly idiopathic in girls. Needless to say, when this occurs in little children, the psychosocial implications are profound and the effect on the parents is devastating. These children at presentation are significantly taller than their age matched peers and have secondary sexual characteristics and an advanced bone age. The treatment for this condition is to halt the progression of puberty by blocking the effect of gonadotrophins on the gonads. This is achieved with gonadotrophin releasing hormone analogues (GnRHa) injected 4 weekly. Unless treated effectively, apart from the psychosocial effects, these initially tall children become very short adults due to early epiphyseal closure.

We are treating 15 children with CPP, 12 of whom are girls[17]. The youngest girl presented at 1 year and youngest boy at 1 year and 3 months. All three boys and 1 girl had hypothalamic hamartomas on their MRI scans. In 2009 we studied the growth patterns of 9 girls who have completed 3 years of treatment. Their ages at onset of treatment ranged from 1 year and 5 months to 5 years and 7 months with a mean age at onset of treatment of 3.5 ± 1.46 years. All had normal MRI scans of the brain. Their mean pre-treatment height standard deviation scores (SDS) were compared with mean post-treatment height SDS using the paired t test. We found that the mean height SDS at the end of 3 years of treatment had significantly reduced (0.82 ± 1.08) compared to mean pre-treatment height SDS (2.54 ± 1.48), $t = 7.25$, $p < 0.001$ (Table 6).

Table 6. Assessment of effect of treatment on height of the study population

Serial number	*Pre treatment age (m)*	*Pre treatment height (cm)*	*Pre treatment height SDS*	*Post treatment age (m)*	*Post treatment height (cm)*	*Post treatment height SDS*
1	56	120	3.15	92	135	1.8
2	51	107.2	0.94	87	121	-0.34
3	60	130	4.72	96	140	2.31
4	50	108	1.29	86	121.6	-0.13
5	19	89	2.64	55	106	0.05
6	67	129	3.45	103	138	1.31
7	39	101	1.25	75	121	0.85
8	39	100.2	1.03	75	114.5	-0.47
9	17	91.5	4.38	53	113	2.01
Mean (SD)			2.54 (1.48)			0.82 (1.08)

Statistical significance - $t = 7.25$, $p < 0.001$

Height velocities were calculated before treatment and at 1 year and 3 years after treatment. Statistical significance was determined using the F test or ANOVA. We found that the height velocity too had decreased significantly within one year of treatment and continued to decrease up to the time of reporting after 3 years: F = 5.76, p = 0.008 (Table 7). Bone maturation was analysed as a ratio of chronological age/bone age (CA/BA). A significant increase in CA/BA ratio was observed after 3 years of treatment (0.47 ± 0.08 to 0.71 ± 0.13, t = 21.6, p < 0.001) Table 8. These children will be followed up till treatment is discontinued which will be when their peers go into puberty or earlier if requested. These findings confirm the beneficial effects of specific treatment on the growth patterns of children with CPP.

Table 7. Assessment of height velocities of the study population

Serial number	*Pre treatment velocity cm/year*	*Velocity 1 year after treatment cm/year*	*Velocity 3 years after treatment cm/year*
1	9.0	3.74	2.1
2	1.2	6.8	3.75
3	6.0	4.71	2.04
4	12.9	5.54	3.7
5	19.2	4.36	6.5
6	9.3	13.0	2.2
7	7.3	15.4	4.0
8	17.3	7.2	4.3
9	24.0	6.5	7.8
Mean (SD)	11.8 (7.21)	7.47 (4.02)	3.57 (2.08)

Statistical significance – F = 5.76, p=0.008

Table 8. Assessment of skeletal maturation of the study population chronological age / bone age (CA/BA)

Serial number	*Pre treatment CA/BA*	*Post treatment CA/BA*
1	0.42	0.59
2	0.45	0.93
3	0.61	0.84
4	0.44	0.59
5	0.55	0.61
6	0.47	0.55
7	0.37	0.65
8	0.43	0.69
9	0.55	0.67
Mean (SD)	0.47 (0.08)	0.71 (0.13)

Statistical significance - t = 21.6, p<0.001

Are we really doing our best for these children? Assessing 'client satisfaction'

In the days gone by doctors were treated with the utmost respect and even reverence. Unfortunately things are different now. Ever so often there are remarks in the newspapers about us which are not at all complimentary![18] I think that at all times, we do our best for the patients with the limited resources that are available to us in the government hospitals. Whatever appears in the print media, as a paediatrician I think the best person to ask about what we do, would be the mother who is invariably with her sick child in hospital[19]. Even when attending the clinic for follow up, the mother almost always comes with her child. Therefore we asked them what they really thought of us and the service they received at the endocrine clinic at LRH.

This clinic came into existence in October 2001 and is held twice a month. There are 30 - 40 children at each clinic seen by the consultant, senior registrar and 2 to 3 registrars. Our objectives of doing this study were to document the parents' views regarding: education received about their children's conditions, interaction with the doctors, meeting parents of children with similar conditions and problems encountered in attending the clinic. We did a descriptive, cross-sectional study in May 2007[20]. A self-administered questionnaire was given to 100 consecutive mothers of new and follow-up patients. Questions were tailored to realise the objectives of the study and the responses to the questions assessing mothers' satisfaction regarding aspects of care provided were graded on a scale of 4: strongly agree, agree, uncertain, no comment.

Sixteen were new patients and 84 were children being followed up. Fifty nine were girls. Fifty three were below 10 years of age. Sixty two children were from the Western Province. Education up to ordinary level and higher had been received by 83 mothers and 50 families had a monthly family income of less than Rs 10,000.00. Commonest condition in these children was congenital hypothyroidism (Table 9a). Sixty three mothers strongly agreed that they received adequate education about the condition while 57 of 97 (59%) and 74 of 97 (76%) respectively, strongly agreed that the doctors knew almost everything about their child and that they examined the child carefully. Fifty seven of 84 mothers (68%) wished they had longer time with the doctors. All of them agreed that they were satisfied with the overall care their children received at this clinic. No comment was given by 11 mothers out of 93 who responded (11.8%) regarding forming support groups. Although they had financial problems coming to Colombo, they were very satisfied with the management and care they received at this clinic (Table 9b).

Table 9a. Socio-demographic features of the study population (n = 100)

A			
Patients	*New: 16*	*Follow up: 84*	
Gender	*Girls: 59*	*Boys: 41*	
Age (years) (n=84)	≤ 5: 26	5-10: 27	>10: 31

B	**Area of residence – Province**
	Western: 62
	Southern: 8
	North Western: 12
	Central: 2
	North central: 3
	Uva: 2
	Sabaragamuva: 11

C	**Education level of mothers**	**n=100**
< Grade 5		2
Grade 5 - 10		15
O' Level		48
A' Level and higher		35

D	**Monthly family income (Rs)**	**n=100**
	Income (Rs)	*Number*
	< 5000.00	17
	5 - 10,000.00	33
	10 - 20,000.00	35
	> 20,000.00	15

Table 9b. Parents' views of the care received at a specialized clinic

Items in questionnaire	*Responses*			
	Strongly agree	*Agree*	*Uncertain*	*No comment*
'Received adequate education about condition' (n=100)	63	36	-	1
'Doctors know almost everything about my child' (n=97)	57	35	2	3
'Doctors examine my child carefully and completely' (n=97)	74	23	-	-
'I am very satisfied with the medical consultation my child receives at this clinic' (n=95)	60	35	-	-

Wish for longer time with the doctors (n=83)

Agreed – 57 (68.7%)

Disagreed – 11 (13.3%)

No comment – 15 (18%)

To further improve the care given, the endocrine clinic must be a truly multidisciplinary clinic with services of a paediatric surgeon and child psychiatrist and ideally a social worker, enabling us to do a lot more with less inconvenience to the parents.

Plans for the future: Ongoing studies

Disfiguring hormones

We have several children, both boys and girls being treated for CAH (illustrations). They are managed mostly based on clinical assessments (4) and are doing well. We are in the process of collecting data to document the outcome of medical management in both sexes and surgical outcome regarding appearance and function after reconstructive surgery in the girls. Psychological impact on parents and older children are also being assessed[21].

Little brains devoid of hormones

Thyroxine is not essential for life. But life is not worth living without thyroxine. This is vividly documented by this statement about treatment with thyroxine: 'Not the magic wand of Prospero or the brave kiss of the daughter of Hippocrates ever effected such a change as that which we are now enabled to make in these unfortunate victims, doomed heretofore to live in hopeless imbecility, an unspeakable affliction to their parents and their relatives' – *William Osler 1897*.

Although the physical manifestations improve, significant neuro-developmental and intellectual deficits remain unless treatment is started as early as possible after birth. Over the years numerous studies have been done on various aspects of congenital hypothyroidism. Presently we are studying the effect of congenital hypothyroidism on the growth, neuro-development and behaviour aspects in a cohort of such children attending the endocrine clinic at LRH[22]. We are also evaluating the impact of defined predictors to the above outcome identified in previous studies: age at diagnosis, initial thyroxine level, commencement dose of thyroxine and frequency of clinic follow up. Comparison groups are 100 age and sex matched healthy children from a primary health care centre and 2 urban schools. Neuro-developmental assessment is done in the areas of gross motor, fine motor, language and cognition in different age groups using different tools.

Children 0-4 years old are assessed using Bayley infant scales and Griffith development scales modified to be used with Sri Lankan children are used in children 4 - 7 years of age. Assessment of 7-10 year old children is by using a locally validated skills assessment tool presently used in all national schools. Behaviour assessment is by a self-administered questionnaire given to parents of children over 5 years of age. This is based on the Strengths and Difficulties Questionnaire validated to be used in our children. We have studied 22 patients so far, 15 girls and 7 boys aged 6 months to 11 years.

The journey continues…

This is just a glimpse into the mysterious world of hormones. Much more can be said about these

chemicals which, due to a lack or an excess, can cause havoc on the physique and psyche of a growing and constantly changing child. Likewise, the magical effects of replacement are indescribable. Time does not permit me to reflect and ramble…

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