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by *D.F. Swaab, Netherlands Institute for Neuroscience, Amsterdam, the Netherlands.*

Welcome

We warmly welcome you to Wellington, New Zealand, to our first Asia/Pacific Prader-Willi Syndrome Conference which has come about by the desire of both the Australian and New Zealand PWS Associations to broaden our Australasian triennial conferences to include our neighbouring Asian countries. We hope, in the future to share the responsibilities of hosting these conferences among participating countries.

It is our desire – and that of our International PWS Organisation (IPWSO) – to increase awareness of PWS to a greater level in geographic regions and by doing so give countries the opportunity to not only hear world-renowned speakers, but have their own speakers address all fields of research. In the world of PWS, things change rapidly and we need a strong forum in which to discuss and learn.

"Broadening Horizons and Making Connections" is our theme for this First Asia/Pacific Conference and we hope that you all have the opportunity to build new friendships, strengthen and renew old ones, make new connections, and increase your knowledge of Prader-Willi Syndrome and look to the broad horizon where new discoveries are bound to lie.

Linda Thornton
National Director, PWSA (New Zealand)

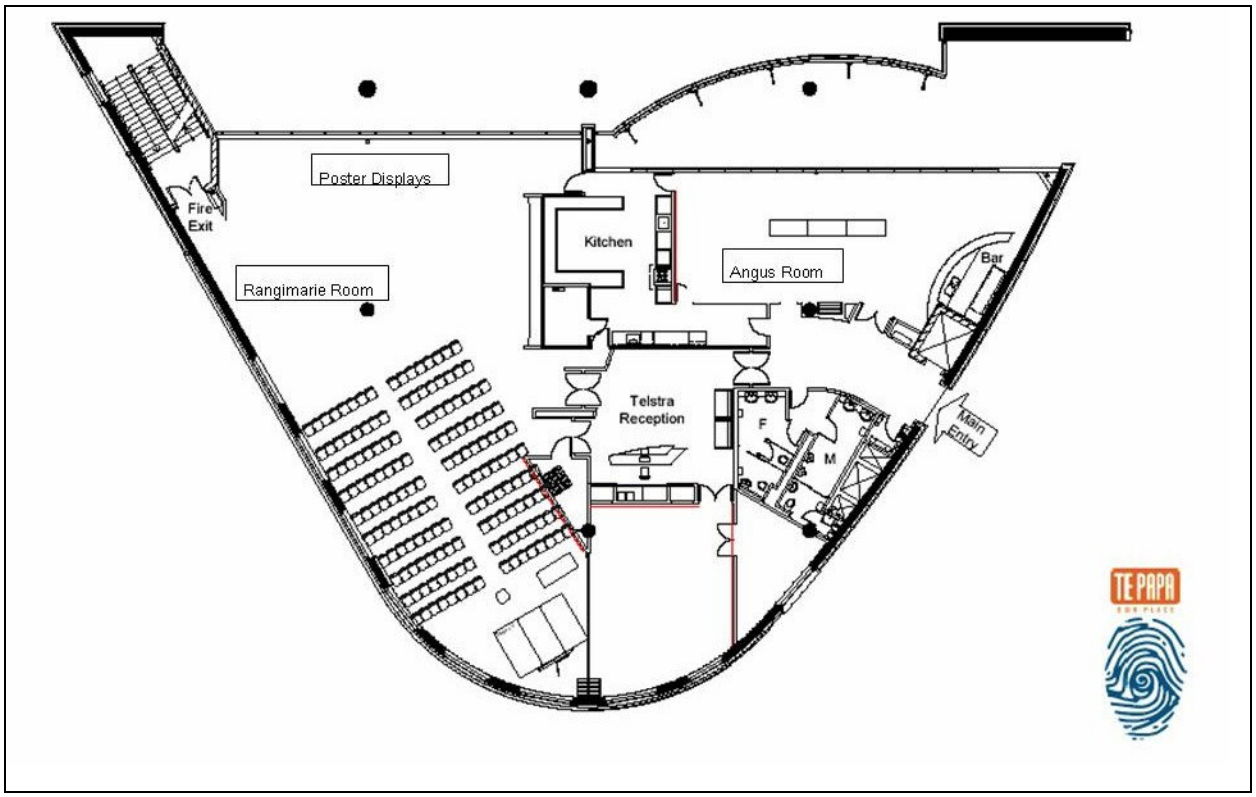
On behalf of the organising committee:

Barry Greensmith, President PWSA (Australia)
Helen Anderson, PWSA (Australia)
Nick Thornton, Treasurer, PWSA (New Zealand)
Georgina Loughnan (Australia)
Peter Davies (Australia)

and advisers:
Paul Hofman (New Zealand)
Tomoko Hasegawa (Japan)

Registration and General Information

The main rooms for the conference will be in the TelstraClear Centre: Rangimarie Rooms 1 & 2 for all plenary sessions, and, on Sunday, the Icon Room (directly below the TelstraClear Centre on level 3) will be used for break-out sessions.



Registration Desk

There will be early registration on Friday evening at the Museum Hotel, ground floor foyer. Registrations will also be taken on Saturday morning from 8.00am at the conference registration desk located at the entrance to the TelstraClear Centre, Te Papa, on the fourth floor. The desk will be open from 8.00 am on Saturday and will be open periodically during the conference for enquiries

Name tags

Nametags are to be worn at all times by conference registered delegates. A colour coding system for the lanyards has been used to help you distinguish between delegates, professionals, speakers, and the Organising Committee.

Green:	Speakers
Red:	Parents
Blue:	Professionals
Yellow:	Conference Committee

Meals and refreshments

Morning and afternoon tea and buffet lunches will be served from the Angus Room and delegates are encouraged to mix and mingle at the back of Rangimarie Room where Posters will also be on display. There will be a chance to talk to Poster authors will be during lunch times.

Conference Dinner

Saturday: Pre-dinner drinks will be held at the Signs of a Nation, followed by a guided tour through the Manu Whenua, the Maori exhibition section of Te Papa, and the conference dinner will be held on Te Marae.

Cellphones

You are kindly requested to have your cellphone turned off while in any of the conference sessions or workshops.

Pharmacy/Chemist

The closest pharmacy to Te Papa is the Capital Pharmacy in Courtenay Central (in the Reading Centre). Tel: 04.384 8333

Emergency Medical Assistance

Emergency medical services are available on a 24 hour, 7 day basis at Wellington Hospital, Riddiford Street, Newtown. Tel: 04.385 5999

Taxis

Wellington Combined Taxis	04 387 4444
Corporate Cabs	04 387 4600
Airport Super Shuttle	04 387 8787 (0800 Shuttle)

Parking

Covered and uncovered carparks are available at Te Papa. Daily Maximum: $12.00

Rental Cars:

Avis Rent a Car	0800 655111
Budget Car Rentals	0800 283 438
Hertz Car Rentals	04 384 3809

Programme

Friday 29 February

Registration – Museum Hotel Foyer

- Evening registration from 5pm to 7pm at the reception area of the Museum Hotel (across road – adjacent – from Te Papa). Mix and mingle at the bar.
- Registrations will also be taken on Saturday morning at Te Papa.

Saturday 1 March

Rangimarie Room – Te Papa

7.30 – 9.00am **Registration Open**

Morning Session Chair: Esko Wiltshire

- ***Note: Please leave your written questions with the Chair of each of today's sessions. These will be answered by a panel at the end of the day***

9.00 – 9.30am **Welcome**
Shuan-Pei Lin, Vice President, International Prader-Willi Syndrome Organisation (IPWSO)
Opening Talk: When Care becomes a Political Tennis Ball – the importance of a good serve!"
Paul Hofman, President, PWS (NZ) Association

9.30 – 10.30 **"Where are we at?"** *Countries' research and development*
Shuan-Pei Lin (Taiwan)
Ellie Smith (Australia)
Tomoko Hasegawa (Japan)
Warwick Smith (New Zealand)

10.30 – 11.00 **Morning Tea – Angus Room and Rangimarie Room**

11.00 – 11.30 **Genetics of Prader-Willi Syndrome** *Merlin Butler (USA)*

11.30 – 12.00 **Medical Awareness: including hot topics of gastric necrosis, gastric bypass** *Ellie Smith (Australia)*

12.00 – 12.30pm **The Role of Hormones in Appetite** *Alex Viardot (Australia)*

12.30 – 1.30 **Lunch and Poster Presentations, Rangimarie Room**

Afternoon Session Chair: Paul Hofman

1.30 – 1.50 **Sleep Disorders and Endocrine Interactions in PWS**
Patricia Crock (Australia)

1.50 – 2.10 **Assessment of Sleep and Breathing in Adults with PWS**
Brendon Yee (Australia)

2.10 – 3.00 **Growth Hormone Treatment in PWS**
Urs Eiholzer (Switzerland)

3.00 – 3.20 **Growth Hormone in the Adult with PWS** *Charlotte Hoybye (Sweden)*

3.20 – 3.40 **Weight Management and Energy Expenditure**
Peter Davies (Australia)

3.40 – 4.00 **Afternoon tea – Angus Room and Rangimarie Room**

Afternoon Session Chair: Ellie Smith

4.00 – 4.30 **The Paradox of PWS: a genetic model of starvation**
Tony Holland (UK)

4.30 – 4.50 **Frequency of Severe Scoliosis in PWS**
Toshiro Nagai (Japan)

4.50 – 5.10 **Measurement of Para-Vertebral Muscle Volume in Scoliosis** *Nobuyuki Murakami (Japan)*

5.00 – 5.30 **Question/Answer Panel**

Social

6.30 – 7.30 **Pre-dinner drinks with hors d'oeuvres at Signs of a Nation**
7.00 – 7.30 **Short guided tour of Manu Whenua, then walk through to Te Marae for buffet dinner**
7.30 onwards **Dinner**

Sunday, 2 March

Morning Session Chair: Linda Thornton

9.00 – 9.45 **Further and beyond growth hormone therapy - comprehensive care of PWS** *Urs Eiholzer (Switzerland)*

9.45 – 15.00 ***Concurrent Sessions:***
(a) Glucose regulation, diabetes and the metabolic syndrome *Paul Hofman (New Zealand)* ***Rangimarie Room***
(b) Hormones for Adults *Kate Steinbeck (Australia)* ***Icon Room***

10.15 – 10.45 **(a) Exercise & Development in Children** *Peter Davies (Australia)* ***Rangimarie Room***
(b) Exercise & Wellbeing for Adolescents *Georgina Loughnan (Australia)* ***Icon Room***

10.45 – 11.00 **Morning Tea**

11.00 – 11.30 **(a) Nutrition for Children - Reading Labels** *Peter Davies (Australia)* ***Rangimarie Room***
(b) Nutrition for Adults – Is Nutrition Missing from the Diet? *Janet Franklin (Australia)* ***Icon Room***

11.30 – 12.30pm **(a) "Is this the right room for an argument?" Behaviour in the younger child** *John Ford (NZ)* ***Rangimarie Room***
(b) Medication in the treatment of behaviour and ethics of food control *Tony Holland (UK)* ***Icon Room***

12.30 – 1.30 **Lunch – Poster presentations**

Afternoon Session Chair: Shuan-Pei Lin

1.30 – 2.00 **Prader-Willi Syndrome: Evidence Supporting an Autistic Spectrum** *Merlin Butler (USA)* ***Rangimarie Room***

2.00 – 2.30 **Understanding routines, repetitive questions and temper outbursts in Prader-Willi Syndrome** *Chris Oliver (UK)* ***Rangimarie Room***

Concurrent Sessions

2.30 – 3.00 **(a) Alternative Therapies: open discussion group:** *Urs Eiholzer (Switzerland) Peter Davies (Australia) Helen Anderson (Aus) Janet Franklin (Aus)* ***Rangimarie Room***

(b) "Is this the right room for an argument?" Behaviour as a form of communication in the older person *John Ford (NZ)* ***Icon Room***

3.00 – 3.30 **Afternoon Tea**

3.30 – 4.30 **(a) Schooling options** *Helen Anderson (Australia)* ***Rangimaire Room***

(b) Residential Options

- Some Reflections on Developments in Residential Services for People with Prader Willi Syndrome *Angus Capie (NZ),*
- Service Delivery: Strategies that Deliver Quality of Life *Anna Hughes (Australia)* ***Icon Room***

4.30 – 5.00 **The Power of Positive Attitudes** *Linda Thornton on behalf of Pam Eisen (USA)* ***Rangimarie Room***

Conference ends

Pam Eisen with young friend
at the 6th International PWS Conference
in Romania, June 2007

Abstracts – Oral Presentations

in order of programme

Where are we at? Status quo and the Supportive System in Singapore, Thailand and Taiwan

Shuan-Pei Lin[1,2,3], *PWSA-Taiwan, PWSA-Singapore* and *PWSA-Thailand*
1. Departments of Pediatrics and Medical Research, Mackay Memorial Hospital, Taipei, Taiwan; 2. Department of Early Childhood Care and Education, Mackay Medicine, Nursing and Management College, Taipei, Taiwan; 3. Department of Infant and Child Care, National Taipei College of Nursing, Taipei, Taiwan.

The very first Prader-Willi syndrome (PWS) patient in Taiwan was diagnosed in 1990. However, the needs to provide a comprehensive supportive network for the PWS patients and their families were not fully recognized until recent years. The launch of our National Health Insurance (NHI) Program in 1995, the establishment of the Taiwan Foundation for Rare Disorders (TFRD) in 1999 and the legislation of the Rare Diseases and Orphan Drugs Act in 2000 bring great impacts to the caring system for PWS individuals in Taiwan. The formation of PWS family group in 2001 and their active promotion ever since led to the founding of PWSA-Taiwan 4 years later. All these important events work together and exert a great power to pave the way for long-term support and care of the PWS patients and their families.

Up to December 2008, there are 143 PWS patients being identified through the nationwide reporting system and self-contact with the association. Among them, 79 are male and 64 are female, 30 are older than 15 years and 5 deceased. The implementation of referral network and free screening for PWS helps a great deal in early diagnosis and early management, and that makes a big difference.

Thailand has its PWSA founded in 2003 and the PWS Support Group was formed in 2004 in Singapore. Forty seven and 19 patients/families are recruited as members in Thailand and Singapore, respectively. National Health Service Organization (NHSO) of Thailand endorses HGH treatment only for those proved to have growth hormone deficiency. PWS families have to pay for the HGH treatment all by themselves and only 4 patients have had the therapy. Basically, help from the society and the governmental support still need to be enhanced.

The main problems we currently face are learning disability, eating disorders, behavioral problems, coping with family members and classmates, interaction with the society, and unstable physical status in the families with school-aged and older PWS patients. As for the newly diagnosed patients, social and psychological supports are the most wanted. Through education and continuous support from a comprehensive group of medical professionals, social workers, NHI Bureau, PWSA-Taiwan and TFRD, most of the families and their PWS child are standing up and well-prepared to step forward to face the special destination in their life.

There's always room for improvement. Our future goals are as follows:

- Earlier diagnosis & earlier intervention
- Continuous parent & family education
- Psychological support & crisis services
- Arousal of more awareness from professionals
- Arousal of more awareness from the society
- Well-organized follow-up system
- Residential/shelter homes for adult PWS individuals

Where are we at – Australia

Ellie Smith Department of Cytogenetics, Children's Hospital at Westmead, NSW, Australia.

This topic will be dealt with under 4 headings

Diagnosis

There is no doubt that the diagnosis of PWS in Australia is now very effectively achieved for nearly all cases, certainly those born in any reputable hospital. Virtually any hypotonic baby will have the diagnosis considered as also will obese slow children and a methylation test ordered. Awareness of the syndrome and an effective diagnostic test have enormously improved diagnosis compared with 20 years ago.

Management

The increased awareness has led to the establishment of clinics for PWS in the capital city of every state, in some cases more than one clinic. At these clinics, programs of diet control and exercise regimes are in place, as well as checking for sleep apnoea, cardiovascular and other diseases. Discussions with parents/carers is a fundamental component of the clinic program.

Research

Is ongoing in several centres, including snoRNAs, energy metabolism, satiation and growth hormone studies. Several groups are doing their "own" research, usually on small numbers, resulting in inconclusive data. Research in Australia could be much better – with more collaboration. I believe that we are missing out here.

Repository

The need for comprehensive data collection and keeping each other informed is being addressed.

Where we are in Japan

Tomoko Hasegawa, Clinical Geneticist, Genetic Support and Consultation Office, Japan

In Japan the prevalence and incidence rates of various genetic types of PWS are the same as in other countries. Lately, in most children with the deletion type PWS, diagnosis has been made shortly after birth because they are easily identified by their light skin color and light brown or even blond hair, but so far the parents have been given information only on future obesity, and no other supportive help. Physicians usually recommend early intervention, but without an understanding of PWS, positive effects are not achieved. If the children are fortunate, they see physicians or dentists who are knowledgeable in PWS. However, a lot of people with PWS aged over thirty may be left undiagnosed. Though there is no systematic approach in Japan, trials are made in some districts and medical institutions.

Medical, nutritional and / or dental approaches:

Many medical professionals and dentists attend the patients with PWS properly, but with little cooperation from others. The children who are fortunate get physical therapy to improve muscle tone and movement, occupational therapy for coordination and fine motor skills and/or speech therapy for their articulation. Few psychologists are interested in PWS, so I am trying psychotherapy (cognitive behavior therapy). Some are doing music therapy, art therapy, and/or dance therapy.

- Dental care includes advice on weaning for chewing well and increasing saliva. For the prevention of dental caries, tea is used in our country because tea included fluorine and catechin.
- Only Dietitians at the children's hospitals work with patients with PWS.
- Some medical scientific research is performed also in Japan, for instance

endocrinological studies and brain research using high - field MRI system.

- Social and governmental understanding and acceptance

Generally, most people including teachers, social welfare workers, police officers and government officials in our country know little about PW. To increase awareness of PWS, Eiko Shoji who has a son with PWS and is the Secretary-General of PWSA Japan, haunts the government offices, hospitals, schools and so on. But most Japanese parents tend to depend on the government and accept their fate with resignation. It is unbeneficial for their children and themselves, and it is not democratic. Therefore we will begin to do parental education using a way of workshop.

Many district nurses are eager to care for the people with diseases or disabilities. This may be the best way for people with PWS. Dr. Miyako Kawamura, attending the conference, is also working with district nurses. Some people with PWS are living group homes, but it is sometimes difficult to live with other people without PWS. Group homes appropriate for PWS may be required. There are an adult who lives in an apartment with daily care by a social welfare service.

Employment: many people are working in sheltered workshops, but as far as I know, getting jobs are not unusual, such as a special school (as a helper), a chicken yard, grooming shop for the dogs, illustrator for circulars, etc.

Support groups: In Japan there are several parent groups and the PWSA Japan. PWSA Japan is a young support group started in 2005 and at present 68 parents from families and 12 professionals including 8 physicians and a dentist are members.

A State of the Nation of PWS in NZ

Warwick Smith, General and Developmental Paediatrician, , General and Developmental Paediatrician at Kidz First at Middlemore Hospital, Auckland

Due to a low return rate of survey questionnaires (26 of 80 mailed to members of the NZ PWS support group), only a semi-quantitative analysis could be performed. PWS individual's ages ranged from 2 to 38 years. Ten had a deletion, 8 UPD, one IC defect and 7 unknown. Individuals younger than 20 years of age were primarily diagnosed by 2 years of age, while older individuals were most commonly diagnosed during the school years. Obesity is a significant health problem occurring in almost all from school age. Most PWS individuals of all ages receive no ongoing professional support for weight reduction. Daytime tiredness is a common symptom for all ages, while snoring is very common in the older group. Sleep studies have been performed in many younger, but not older individuals. Most have eye problems, while only a few have had hearing problems. Scoliosis occurs in a third; a third of these needed surgery. A third also underwent orchidopexy and only one was unsuccessful. Orthodontic concerns are common. Almost all under 18 years have or do receive either developmental or acadaemic support. Behaviour problems are very common, especially oppositionality, rages, anxiety and compulsions. Three had experienced psychosis and two have suspected autism. Medications, especially SSRI, were prescribed for some. GH treatment is still the exception. Many adults undertook voluntary or part-time work. Almost all over 20 years of age live in a residential situation. The level of satisfaction with health, education, NASC and WINZ services varied widely, but was generally low to moderate. However most individuals were happy/contented with their life.

Genetics of Prader-Willi Syndrome

Merlin G. Butler, MD, PhD Kansas City School of Medicine, USA

Prader-Willi syndrome (PWS) is a complex neurodevelopmental disorder characterized by infantile hypotonia and feeding difficulties, hypogonadism and hypogenitalism, hyperphagia and onset of obesity in early childhood, small hands and feet, mild mental deficiency, behavior problems (skin picking, temper tantrums, stubbornness) and a characteristic facial appearance (small up-turned nose, narrow bifrontal diameter, strabismus, down-turned corners of the mouth and almond-shaped eyes). Additional findings include short stature, scoliosis, dental abnormalities, endocrine disturbances such as growth hormone deficiency and diabetes mellitus, sleep apnea and co-morbidities related to obesity. In addition, preliminary pre- and post-meal brain imaging studies using functional MRI of a cohort of individuals with Prader-Willi syndrome and controls have revealed post-prandial hyperfunction in the limbic and paralimbic cortical regions of the brain in PWS. This failure of association and lack of satiation following a meal appears to have a neurological basis in Prader-Willi syndrome.

PWS arises from lack of expression of paternally inherited genes known to be imprinted and located in the chromosome 15q11-q13 region. A *de novo* paternally derived chromosome 15q11-q13 deletion is seen in about 70% of cases, maternal disomy 15 in 25% and the remaining individuals have either genomic imprinting defects (microdeletions or epimutations) of the imprinting center or chromosome 15 translocations. Thus, PWS is considered a contiguous gene syndrome with evidence from mouse models that a deletion of any of the three imprinted genes (MAGEL2, NDN, or the snoRNA cluster) can cause neonatal lethality, failure to thrive or features of PWS. The function of snoRNAs in the 15q11-q13 region is unknown but sequence complimentarity of some of the snoRNAs to structural genes (e.g., HBII-52 and serotonin receptor HTR2C gene) suggests a role in processing of specific messenger RNAs which may play a role in the PWS phenotype.

Individuals with PWS with the typical chromosome 15 deletion are more homogeneous in their clinical presentation compared with maternal disomy. There are two recognized typical deletions (Type I and Type II) with more recognized behavior problems including self-injury and intellectual impairment in those with the larger Type I deletion (average size = 6.5 Mb) with breakpoints at BP1 and BP3 in the 15q11-q13 region compared with those having the smaller Type II deletion (average size = 5.3 Mb) with breakpoints at BP2 and BP3. In addition, those with maternal disomy may be at a higher risk for developing psychosis. Gene expression studies with microarray technology using lymphoblasts from PWS subjects and whole brain samples from mice with the PWS equivalent genetic defect show disturbed gene activities in candidate genes inside and outside of the PWS chromosome region supporting a causative role. Several of these genes are involved with neuroregulation, appetite and metabolism (e.g., OXTR, HTR2C, POMC, HCRT, STAR). These disturbances may lead to abnormal brain development and function detected in this syndrome. Genomic and proteomic tools will undoubtedly identify more interactive genes outside the 15q11-q13 region impacted by the loss of imprinted genes in the 15q11-q13 region leading to the Prader-Willi phenotype.

Medical Awareness: including hot topics of gastric necrosis, gastric bypass

Ellie Smith, Department of Cytogenetics, Children's Hospital at Westmead, NSW, Australia.

The high mortality and morbidity rates in Prader-Willi syndrome (PWS) are well documented. Prevention of the problems is the aim of good management, but this can only be achieved by knowing ahead where the potential problems lie and then instituting measures to counteract them. The well known morbidity associated with extreme obesity, lack of exercise, poor circulation and respiratory illness – the cardiovascular-circulation morbidity – is one thing. Other morbidities also occur, not so well known. This includes the dangers associated with gastric necrosis and gastric bypass. In this presentation, adverse symptoms, signs and behaviours will be flagged, so that management can be alerted before serious problems arise.

The Role of Hormones in Appetite

Alexander Viardot Endocrinologist, FRACP, Garvan Institute of Medical Research Sydney

Prader-Willi syndrome (PWS) is a genetic disorder characterised by insatiable appetite, hyperphagia and severe obesity from early childhood. The cause of this disturbed appetite regulation is still poorly understood, and is thought to arise from abnormal development of the hypothalamus and/or hormonal disturbances. In the last decade we have seen significant advances in research trying to understand how appetite and metabolism are regulated by the gut and brain, and a number of gut-derived hormones have been discovered and characterised which have a major impact on inducing hunger or satiety. This has triggered further research and early clinical trials to understand the mechanism of development of obesity. An increasing number of these hormones have now been studied in PWS, with the aim to investigate whether an imbalance of these appetite regulating hormones is responsible for increased appetite in PWS and could serve as therapeutic target.

The phenotype of PWS includes a lower lean body mass, lower central fat mass and a greater insulin sensitivity with low insulin levels, as compared to obese non-PWS individuals. Adiponectin, an adipocyte-derived hormone which is significantly decreased in simple obesity, has been shown to be elevated in PWS to similar levels as seen in lean subjects, and might contribute to the preserved insulin sensitivity.
PYY is an anorexic hormone produced by the gut in response to food, and it has been investigated in several PWS studies investigating whether abnormal levels could explain increased appetite. Results of these studies are contradictory, and our group is trying to find an answer by using newly developed, improved hormone assays.
Pancreatic polypeptide (PP), another anorexic hormone, has been described to be low in PWS both fasting and postprandially, but its role in hyperphagia in PWS is still unclear.
The orexic hormone ghrelin is elevated in PWS, and it is possible that this contributes to the increased appetite. This is in contrast to simple obesity where ghrelin levels are low, probably reflecting a physiological adaptation. Drugs antagonising ghrelin have been shown to cause weight loss in animal studies, and more ghrelin antagonists are being developed for the use in humans.
Glucagon-like peptide 1 (GLP-1) is a hormone produced by the gut in response to food, which enhances insulin secretion and suppresses appetite. GLP-1 levels have been measured in only 1 study so far, and will be further explored in our current trials.
The GLP-1 agonist Exendin-4 (Byetta®) has been released on the market for the treatment of type 2 diabetes. It has significant appetite suppressing and weight reducing effects, and

interestingly, it has been shown to suppress ghrelin levels dramatically. Thus, we have just started a pilot study using Byetta in PWS, looking at changes in appetite/satiety and hormone levels, initially in response to a single dose. If it proves to be effective a large scale study has to be performed before it can be safely used in PWS.
Our collaborators from the Neuroscience Research Program at the Garvan Institute recently described the newly discovered anorexic hormone Macrophage inhibitory cytokine-1 (MIC-1), which is elevated in many cancers and promotes anorexia and weight loss. It was suggested that MIC-1 is a newly defined central regulator of appetite and a potential target for the treatment of both cancer anorexia and weight loss, as well as of obesity, and our group has already started to investigate the role of MIC-1 in PWS.

Sleep Disorders and Endocrine Interactions in PWS

Patricia Crock, Associate Professor, Staff Specialist, Head, Dept of Paediatric Endocrinology and Diabetes, John Hunter Children's Hospital, Newcastle, NSW 2310 Australia

Prader-Willi syndrome (PWS) is a complex genetic condition that leads to hypothalamic endocrine dysfunction associated with respiratory disorders during sleep as well as neurocognitive and behavioural/psychiatric manifestations. It is well recognised that many children have biochemical and/or physical signs of growth hormone deficiency (GHD) and hypogonadism. Adrenal insufficiency has not been widely attributed to this condition, although sudden death is a known complication of PWS. The interplay between endocrine imbalances, weight and breathing issues will be discussed.

Sleep related disorders are extremely common if not universal in PWS, and can be thought of as either centrally mediated (central apnoeas or hypopnoeas) or obstructive. The fact that central and obstructive apnoeas are not completely independent entities adds another layer of complexity. Children with PWS have reduced arousal and ventilatory responses to low oxygen (hypoxia) or high carbon dioxide (hypercapnoea) levels compared to other children. These features are exacerbated by low muscle tone which reduces chest wall movement and worsens obstructive respiratory symptoms. Low muscle tone is partly due to growth hormone deficiency. Studies have shown that growth hormone therapy can improve tone and thus improve ventilation. Untreated growth hormone deficiency and hypogonadism contribute to obesity, which in turn can lead to or exacerbate obstructive sleep apnoea.

Patients with severe obstructive sleep apnoea (OSA) can develop a component of central hypoventilation. The mechanism is poorly understood. However, if the obstruction is treated, the central component frequently resolves. In PWS, the obstructive component is multifactorial including: obesity, poor muscle tone and tonsillar enlargement. Significant OSA has been proven to be associated with impaired academic performance as well as having adverse effects on mood and daytime behaviour.

Hypersomnolence (excessive daytime sleepiness) is a common feature of PWS but is only partly attributable to obstructive sleep apnoea. The aetiology is under investigation.

Growth hormone therapy has been associated with the development of obstructive sleep apnoea. Growth hormone (GH) stimulates the growth of the lymphoid system, including the tonsils. Tonsillar growth can lead to obstructive sleep apnoea and has been postulated as a possible cause of sudden unexpected death in PWS. It is now recommended that a full sleep assessment and assessment of tonsillar size be done prior to starting and during GH treatment.

In summary, sleep disorders and endocrine dysfunction in PWS are closely interlinked. Close collaboration between the Paediatric Endocrine and Paediatric Respiratory and Sleep Medicine teams is important part of management.

Assessment of sleep and breathing in adults with Prader-Willi syndrome: a case control series

Brendon Yee, Consultant Physician, Respiratory and Sleep Medicine, Sydney, Australia

Objectives: Prader-Willi syndrome (PWS) is a genetic disorder (linked to chromosome 15q11-13) characterized by hypotonia and developmental delay, hyperphagia and obesity, hypersomnia and abnormal sleep, and behavioral problems. Such patients may also be at increased risk of obstructive sleep apnea (OSA), although whether this risk is explained by known risk factors has not previously been directly tested. Our aim was to compare sleep and breathing in an older group of patients with Prader-Willi syndrome with a control group—matched on the basis of age, sex, and body mass index (BMI)—in order to determine which specific features are not explained by these known confounders.
Methods: Consecutive patients with PWS attending the PWS clinic at Royal Prince Alfred Hospital Sydney, Australia, were recruited. Age-, sex-, and BMI-matched controls were selected from the Sleep Investigation Unit at Royal Prince Alfred Hospital, and polysomnography-derived sleep and other parameters were compared across the groups.
Results: Nineteen subjects with PWS (14 males) were included in the study. Eighteen (95 %) had a total respiratory disturbance index (TRDI) of greater than 5 events per hour, with 4 (21%) having severe obstructive sleep apnea (TRDI ≥ 30 events/hour) and 9 (47%) having evidence of obesity hypoventilation syndrome. Patients with PWS, as compared with the control group, had evidence of more nocturnal hypoxemia, with lower oxyhemoglobin saturations and percentages of sleep time at less than 80% oxyhemoglobin saturation (all p values < 0.05). There were no significant differences in sleep architecture; however, there was a reduction in rapid eye movement latency seen in the PWS group ($p < 0.05$). Serum leptin was higher than the reference range in the PWS group but was not measured in the control group.
Conclusion: Patients with PWS drawn from an adult and adolescent PWS clinic have a high rate of sleep-disordered breathing. There is evidence that patients with PWS may have more nocturnal hypoventilation than a well-matched control group. These data suggest that the chromosome region 15q11-13 may be involved in some aspects of the regulation of breathing, although whether putative molecular mechanisms act directly or indirectly will require further investigation.

Growth Hormone and PWS

Urs Eiholzer, Associate Professor, University of Zurich, Head of "Centre for Pediatric Endocrinology, Zurich, Switzerland

Prader et al. already presumed that a hypothalamic dysfunction may cause many of the features of Prader-Labhart-Willi syndrome (PWS), including growth hormone (GH) deficiency. Increased fat mass in PWS is accompanied by a decrease in muscle mass as well as short stature resembling the condition of chronic GH-deficiency – this is in contrast to simple non-syndromal obesity. The reduction of muscle mass being present at early childhood already is the most important disturbance of body composition in PWS resulting in decreased energy expenditure and basal metabolic rate. This again is in contrast to simple obesity. GH treatment studies which were conducted during the past few years showed: (1) The effectiveness of GH substitution in

PWS is confirmed by a sustained improvement of growth pattern, normalisation of body proportions and growth predictions. (2) If nutritional input is not augmented, weight for height becomes normal and body composition is improved in prepubertal children and infants with PWS. However, even if GH treatment is initiated at a very early age, muscle and fat mass do not normalize. (3) Even though muscle mass is not normalised, physical strength and agility are improved. (4) Physical hypoactivity arising from hypothalamic dysfunction however is unchanged on GH therapy which explains why muscle mass does not normalize on GH therapy. (5) GH therapy improves lipid metabolism, does not influence glucose tolerance, but increases levels of DHEAS, a weak adrenal androgen. This GH related effect may add to the premature or enhanced secretion of adrenal androgens (adrenarche) typically seen in PWS.

Growth Hormone Treatment in adults with Prader-Willi syndrome

Charlotte Hoybye Department of Endocrinology, Metabolism and Diabetes
Karolinska University hospital, Solna, 171 76 Stockholm, Sweden

Results of several growth hormone (GH) treatment studies in PWS children have shown improvement in growth, body composition, physical strength and agility. However, the knowledge of GH therapy in adult PWS is limited. So far only one placebo controlled study exists. In this 6 months study of 17 adults with clinical PWS (11 methylation positive), we have shown that compared to placebo, GH treatment significantly decreased body fat. After the initial 6 months all received active GH treatment for 12 months and in the methylation positive individuals a significant reduction in body fat concomitant with a significant increase in lean body mass were seen. Lipid profiles, insulin levels and HOMA index did not change. Side effects attributed to water retention occurred in three patients. In 2005 a follow-up was performed. Ten methylation positive PWS adults from the original study group were examined. Six of them were treated with GH for 5 years. At follow-up BMI was unchanged in the GH treated group, while it seemed to increase in the non-treated group. Body composition had improved in the GH treated group, with a median increase in lean body mass of 5 kg and a median decrease in body fat of 13%, as compared to the non-GH treated group with a change in lean body mass of 0.4 kg and in total body fat of -7%. Only one non-GH-treated woman had developed overt diabetes. Thus, our pilot studies showed beneficial effects of GH treatment on body composition in adult PWS without serious side effects but also that it was possible in a long term perspective to implement GH injections despite behavioural problems.
GH treatment might offer an opportunity to reduce some of the adverse consequences of the PWS syndrome. To settle the definite role of GH treatment in adult PWS studies of larger cohorts are needed.

Weight Management and Energy Expenditure

Peter SW Davies, Director, Children's Nutrition Research Centre, University of Queensland, Royal Children's Hospital, Brisbane, QLD 4029, Australia

Successful weight management in any individual is better achieved with an understanding of the basics of energy balance and the interactions between energy intake and energy expenditure. Indeed, as energy balance in the human is bound by strict laws of thermodynamics, chemistry and physics, some key, but basic knowledge of energy metabolism could be seen as vital in order to fully maximise the chances of successful weight management. Put simply, but appropriately, if more calories are consumed than are expended human metabolism has no option but to store that excess energy, often as body fat. A salient fact here, however, is that it

is relatively easy to consume excessive energy quite quickly, whereas, the equivalent energy expenditure brought about by physical activity takes much longer to achieve. This mismatch is at the core of many cases of energy imbalance and weight gain. It is also important to dissect the energy intake part of the balance further and to realise that not all foods are equal in their calorie densities. One reason for this is that the key macronutrients, namely fat, carbohydrate and protein differ significantly in their energy densities, with fat containing twice as much energy as an equivalent amount of protein or carbohydrate. In children and adults with Prader-Willi syndrome the energy balance equation can be further compromised by the fact that disturbances in body composition mean that when considered on a body weight basis the actual energy needs of such individuals are less than those of an unaffected individuals. This does not, however, mean that children or adults with Prader-Willi syndrome have a fundamentally reduced metabolism or metabolic rate. When adjusted for body composition differences, most studies report that the resting metabolic rate is entirely normal.

The Paradox of PWS: A genetic model of starvation

Holland, A., Whittington, J., Hinton, E. (2003).The paradox of Prader-Willi syndrome: a genetic model of starvation. The Lancet, 362, 989-991.

Since PWS was first reported in the literature in 1956, our understanding of one of the most significant problems associated with the syndrome - that of life threatening obesity - has changed substantially. The risk of obesity is now seen as a direct consequence of a failure of the normal satiety response to food intake, which then results in excessive and continuous eating behaviour if the person concerned is allowed free access to food. Food intake therefore far exceeds the daily and long term nutritional demands of the body, aggravated by the fact that fat stores compared to fat free mass are high in PWS and exercise levels are often low. Thus, 'calories in' markedly exceed 'calories out' and obesity is inevitable.

The task of research is to understand the underlying peripheral and brain mechanisms that result in such abnormal eating behaviour and ultimately to develop treatment and management strategies that ideally will enable the person with PWS to lead an independent life that will not, with such independence, inevitably result in life threatening obesity. Behavioural and brain scanning studies indicate that brain responses to food intake are abnormal in PWS and that those areas of the brain normally associated with 'fullness' (or satiety) appear not to be activated (or are only limitedly activated) even after levels of calorie intake that would normally be fully satiating. Our group have therefore argued that people with PWS are best conceptualised as behaving as if in a continuous state of hunger (Holland et al, 2003). The consequences of this are, as would be expected, that people with PWS have a continuous desire to eat and a hormonal profile (low sex and growth hormones) and low levels of activity that are akin to that observed in states of chronic hunger. The difficulty for people with PWS is that they live in a food rich environment and therefore become obese. Such a 'conceptual model' of the eating behaviour observed in people with PWS allows those of us without PWS to understand more about what it must be like to have the syndrome and guides thinking about treatment and the ethical and legal aspects of support.

Frequency of severe scoliosis and prognosis after surgical treatment of scoliosis in Prader-Willi syndrome

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(Background) The frequency of scoliosis in PWS is known to be high as much as 50 % in Japan. But the frequency of severe scoliosis and the prognosis after surgical treatment have not been known yet. Since the beginning of growth hormone therapy for PWS worldwide, the relationship between GH and scoliosis has been debated. (Purpose) We evaluated the frequency of severe scoliosis and the prognosis of neurological symptoms and height after surgery. (Subjects) 122 patients (77 males and 45 females; 90 deletion type, 31 UPD or IC abnormalities types, 1 complex chromosomal aberration) who have been followed at our outpatient clinic were analyzed. (Results) Fifty patients (41%) were found to have scoliosis with Cobb angles greater than 10 degrees. Of these 50, 8 patients (6.5%) showed severe scoliosis and were listed as candidates for surgical treatment (Cobb angles greater than 60 degrees). Five of these 8 patients underwent surgery (age at operation: 2 to 18 years; surgical methods: anterior vertebral fusion in 3 patients, posterior vertebral fusion with instrumentation in 2 patients). No unfavorable episodes were observed during and after surgery. The duration of follow-up after surgery ranged from 1.6 years to 11 years. None developed neurological complications. The youngest patient who had surgery (at the age of 2 years) was restarted on GH with satisfactory height gain after surgery. One patient who had surgery at the age of 7 years reached a satisfactory final height (140.5 cm, -0.14SD of Japanese PWS females) 11 years after the surgery . Her Cobb angles were 71 degrees before surgery, 21 just after surgery, and 60 at the age of 18 years. Two patients' families refused surgical treatment for scoliosis because of massive obesity in one and an excessively aggressive character in the other patient. One patient is now waiting for surgery. (Discussion) The frequency of scoliosis was 50 out of 122 patients (41%). Eight (6.5%) showed severe scoliosis. Neurological complications developed in none of the 5 operated patients and their height gain after surgery was satisfactory. Six out of these 8 patients with severe scoliosis were also treated with growth hormone during certain periods of their course. (Conclusion) The frequency of severe scoliosis was high in PWS, but the prognosis of neurological symptoms and height after surgical treatment was favorable. The relationship between severe scoliosis and GH use remains to be elucidated.

The measurement of paravertebral muscle volume can be a useful indicator of progression of scoliosis in PWS with GH therapy.

Nobuyuki Murakami, MD, PhD, Kazuo Obata, MD, PhD, Yoshitaka Tsuchiya, MD, Yuriko Tanaka, MD, Yuzo Tomita, MD, PhD, Atsunori Yoshino, MD, PhD, Ryoichi Sakuta, MD, PhD, Toshiro Nagai, MD, PhD, Department of Pediatrics, Dokkyo Medical University, Koshigaya Hospital, Saitama, Japan.

PURPOSE: The purpose of this study was, firstly, to investigate the clinical course of scoliosis in PWS patients with GH therapy and secondly, to examine whether paravartebral muscle volume can be a candidate indicator of the progression of scoliosis in these patients.
SUBJECTS & METHODS: Twenty six patients with PWS on GH treatment (16 males and 10 females, ages ranging from 2 to 16 y/o, deletion type in 19 and UPD type in 7 patients) were evaluated. Observation period ranged from 8 to 40 months. To evaluate the degree of scoliosis, Cobb angles were measured every 6 months during GH therapy. Simultaneously, one slice of

CT scan was obtained at the level of umbilicus to evaluate paravertebral muscle volume.
RESULTS: Fifteen patients never developed scoliosis (no scoliosis group). Scoliosis improved in 3 patients (improved group) and progressed in 8 patients (progressed group). The mean increase of (total) paravertebral muscle volume in each of these three groups were 42.8, 36.0 and 14.7 %/year, respectively.
The mean difference of paravertebral muscle volume of right and left side in the first CT scan were 9.5%, 8.7 % and 9.8 %, respectively. The mean difference of paravertebral muscle volume of right and left side in the latest CT scan were 5.2 %, 5.0 % and 9.5 %, respectively.
DISCUSSION: The clinical courses of scoliosis in PWS patients with GH therapy are variable. Although in many patients scoliosis was exacerbated, improvement was seen in at least some patients. In our study, total paravertebral muscle volume increased more in patients with favorable outcome (no scoliosis group and improved group) than in those with progressed scoliosis (progressed group). Similarly, the degree of asymmetry of paravertebral muscle diminished more in patients with favorable outcome than in those with progressed scoliosis.
CONLUSION: Poor increase of paravertebral muscle volume and/or poor improvement in its asymmetry could be useful indicators for progression of scoliosis in PWS with GH therapy.

Further and beyond growth hormone therapy - comprehensive care of PWS

Urs Eiholzer, Associate Professor, University of Zurich, Head of "Centre for Pediatric Endocrinology, Zurich, Switzerland

Life of children with Prader- Labhart-Willi syndrome (PWS) has dramatically changed since the 90ies, when new therapeutic options were developed. These therapeutic options can be summarized in the 5-finger-model.

1. Restriction of the caloric intake: There is no other way to control weight; controlling weight is the most important aim with major consequences for quality of life, morbidity and mortality in PWS.
2. Growth hormone treatment: There is a growth hormone deficiency in PWS. Replacing Growth hormone helps to reduce weight through its muscle anabolic and lipolytic effect.
3. Daily training program: Physical hypoactivity in PWS arises from hypothalamic dysfunction. We have shown that a daily training program not only improves muscle mass and strength, but increases spontaneous physical activity.
4. Male sex hormone treatment: There is a hypothalamic sex hormone deficiency in PWS. At least in male PWS patients sex hormones should be replaced for two reasons, a) because spontaneous pubertal development is insufficient and b) replacement of male hormones is the most effective improving muscle mass in PWS.
5. Parents need continuous engaged support: Parents of children with PWS are facing many challenges:

   To cope with the handicap; limitation of food intake; increasing physical activity; non-stop surveillance; cope with specific behavior (like skin picking); collaboration and instruction of the network (like teachers) and last but not least – control of numerous care givers. An important issue is protecting people with PWS from arbitrary and needless diagnostic procedures. It is often easier for the modern doctor prescribing new and expensive examinations rather than getting involved in the basic problems – these problems are of high complexity and do need personal commitment and experience. Many parents of persons with PWS have folders full of endless examinations illustrating the so called "qualified" care. But too often the care is not professional and dedicated enough helping

these parents for example fighting 24 hours a day against their child's hunger, which then inevitably leads to tremendous weight gain with all its related complications.

Glucose regulation, diabetes and the metabolic syndrome - a paediatric endocrine perspective.

Paul Hofman, Clinical Director of Paediatric Endocrinology and Diabetes, Starship Children's Hospital, Auckland; Assoc Professor, Liggins Institute, University of Auckland

Children with PWS have an increased risk of numerous diseases, many of which directly related to obesity. One of these is diabetes mellitus which is a relatively frequent occurrence in obese adult PWS (15-30%) but much less common in children and adolescence. Diabetes is usually of two types

1) Type 1 diabetes or childhood diabetes. This is the commonest form of diabetes in childhood and PWS children seem to be at similar risk to the general population with a risk 1:500 in NZ.

2) Type 2 or adult diabetes. This primarily reflects impaired insulin action (also referred to as insulin resistance) the cause of which is usually extreme obesity. However insulin resistance worsens with age, especially after puberty when the sex steroids (oestrogen and testosterone) and growth hormone approximately double insulin resistance. Reduced physical activity is also a major contributor to insulin resistance. This collection of factors results in a greater risk of type 2 diabetes with age, especially after puberty (either spontaneous or induced).

Interestingly PWS are more insulin sensitive than control subjects of similar size meaning they are relatively protected from developing type 2 diabetes. However this protection can be overwhelmed with extreme obesity. There is little data published in children with PWS who develop type 2 diabetes. Personal experience indicates it only occurs in children with extreme obesity and chronic poor dietary control. Where effective dietary management has been impossible to implement, diabetes control is similarly difficult and in the majority of these children diabetes control is poor and deteriorates over time.

Management involves firstly weight loss attempts as dramatic weight reduction can resolve the diabetes and increasing physical activity. If simple life style changes are inadequate oral therapy with an oral insulin sensitizer is initiated followed by subcutaneous insulin use. Regular glucose testing and insulin injections are often very difficult to implement as is a diabetic diet.

Insulin resistance and the secondary elevated insulin levels have been strongly linked to the development of many other metabolic changes which result in adult disease such as hypertension stroke and coronary artery disease. Insulin resistance has also been implicated in the development of excess male hormone in women resulting in excess body hair, irregular periods and acne. The development of these problems in normal obese adolescence is common. Their development in PWS children is much less common although anecdotally it has been noted in extremely obese adolescents with PWS.

This talk will focus on diabetes and the metabolic sequelae related to insulin resistance and discuss management strategies to prevent or manage these.

Hormone Replacement in Adolescent and adult Prader-Willi subjects

Kate Steinbeck, Senior Staff Specialist in Endocrinology and Adolescent Medicine at Royal Prince Alfred Hospital, Sydney.

Hypogonadism (dysfunction of the ovaries or testicles) is one of the major diagnostic criteria for PWS. The majority of males and a high proportion of females will thus have hypogonadism. Hypogonadism is essentially of central origin in females as a result of hypothalamic dysfunction with resulting absence of stimulatory messages from the pituitary to the gonads, and mixed central and peripheral origins in males with cryptorchidism and testicular dysfunction.

Testosterone, the main hormone produced by the testicles and oestradiol, the main hormone produced by the ovaries, are necessary to produce a normal adult physical appearance which is of importance to adolescents and young adults with PWS. In males testosterone will actively increase lean muscle mass as one of its known effects. Oestradiol does not have the same favourable effect on body composition as it is primarily a hormone that influences fat deposition. Both testosterone and oestradiol are important for bone health, in particular to reduce the risk of osteoporosis and bone fracture. In addition low levels of testosterone and oestradiol in young adults appear to increase the risks of early heart disease, a recognized cause of morbidity in adult PWS.
There are a significant number of hormone replacement therapies available which have primarily been developed for the relief of symptoms related to the female menopause and for low testosterone levels in aging males. These are the preparations that will be used for hormone replacement in PWS. In females with a uterus any oestrogen replacement must be given with progesterone in order to reduce the risks of endometrial (womb lining) overgrowth and possible cancerous change. For males, testosterone replacement generally needs to be given as a non-oral preparation. Any medication will have side effects and hormone replacements are no exceptions. In PWS there is often a concern that testosterone will worsen behaviours, although the scientific evidence for this is limited.

This presentation will discuss firstly the benefits of hormone replacement therapy for adolescents and young adults with PWS. The available preparations for hormone replacement will be discussed and the advantages and disadvantages of each of these considered. A protocol for practical hormone replacement based on available evidence and clinical experience will be presented.

Exercise and Development in Children

Peter SW Davies and Kristy Reid, Children's Nutrition Research Centre, University of Queensland, Royal Children's Hospital, Brisbane, QLD 4029, Australia

Children grow and develop at different rates or tempos and there is, therefore, significant variation in physical and mental maturity at all ages in all individuals. This is true for infants and children with Prader-Willi syndrome as well as unaffected children. Exercise and physical activity should play a role in the lives of all children from a young age but in order to take into account the variation in growth and development that occurs in children it is important that age and ability appropriate exercise be prescribed. This presentation will describe such exercise options especially derived and constructed for children with Prader-Willi syndrome which aim to increase energy expenditure and as well as improve muscle tone, endurance, aerobic capacity and strength. Such changes can be useful in day to day activities as well leading to improved quality of life and better outcomes for children with Prader-Willi syndrome. The opportunity will

also be taken to introduce and describe a new resource being developed by the authors that specifically describes exercise interventions that are suitable for children with Prader-Willi syndrome.

Exercise and Well Being for Adolescents & Adults with Prader-Willi Syndrome

Georgina Loughnan, Metabolism & Obesity Services, Endocrinology Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia.

Fitness, good health and well-being are achievable for people with Prader-Willi Syndrome(PWS) through regular, effective exercise. Good health, fitness and strength are essential for a positive quality of life. All clients attending the Royal Prince Alfred Hospital (Sydney, Australia) PWS Clinic, are prescribed both aerobic and strengthening exercise programmes. It has been well proven that exercise will increase energy expenditure, reduce stored fat, increase muscle strength, improve insulin sensitivity, improve blood circulation and cardio-respiratory fitness, decreased stress, protect against bone loss and slow the decrease in general fitness that occurs with ageing. These benefits are essential to people with PWS. Our clients are instructed to exercise daily for muscle strength, and 6 days per week for cardio vascular fitness and weight loss. As a result of a regular, effective exercise regimen, some clients have been able to reduce their medications, for example, for diabetes and hypertension, in association with weight loss and improved cardio-respiratory fitness. Improvements in posture result from strengthening trunk muscles and improved body awareness. Exercise is kept simple, but with a competitive aspect. Clients are encouraged to choose an activity they like that is then tailored to meet their needs and capabilities. Increments of intensity are introduced as the client's fitness improves. Incentive awards are given for achievement. Remembering that people with PWS rely on consistency and routine, exercise, once introduced as a part of the client's individual care plan, can play a vital role in their overall health and well-being. Improved mobility and health, a sense of achievement and better self-worth will assist the client to achieve their full potential. Exercise or planned activity can distract the client from food obsessing, reduce stress and agitation and improve mood. At present, our clinic is looking at physical changes that have resulted from arm strengthening exercises.

Nutrition for Children "Reading Labels"

Peter SW Davies, Director, Children's Nutrition Research Centre, University of Queensland, Royal Children's Hospital, Brisbane, QLD 4029, Australia

There are now statutory requirements relating to food labelling in many countries in the world. The aim, no doubt, is to provide the consumer with information relating to the composition of the food or beverage that he or she is about to consume or provide to others in their care. However, it is clear that many individuals find the information confusing and less than straightforward to interpret. The aim of this presentation to describe food labelling in such a way that provides useful information in relation to energy content as well as some information concerning macronutrient content. Other issues that need to be appreciated relate to the meaning of nutritional claims such as "low fat", "reduced fat", " no added sugar" etc. The opportunity to relate information on food labels to the daily dietary requirements of children with Prader-Willi syndrome will also be explored and described along with fundamental but useful nutritional information that can be gleaned from food labels.

Nutrition for Adults with PWS "Is nutrition missing from the Diet?"

Janet Franklin, Senior Dietitian, Metabolism and Obesity Services, Royal Prince Alfred Hospital, Sydney

People with PWS have a genetic condition resulting in an insatiable appetite, low muscle tone, short stature and a low gag reflex all of which lead to a small requirement for food but a high desire and capacity to eat, and easy weight gain. Obesity has been associated with several co-morbidities such as diabetes, cardiovascular disease, cancers, sleep apnoea, hypertension, high cholesterol, the metabolic syndrome, respiratory conditions and joint and mobility problems. Due to the propensity of people with PWS to being obese and or having higher than expected levels of body fat these co-morbidities are common in this population.
Many adults with PWS are now living in a group home with set menus that are repeated over a one or two week period. Due to their low energy requirements low fat foods, diet foods and bulk foods are often used to make up their regular intake. Conventional treat foods are mostly higher in energy but low in nutrients.
We know that nutrition plays an important role in treatment of cardiovascular disease, diabetes, hypertension and blood lipid profile as well as being important for general well being.
This talk discusses the importance of food variety, how this is achieved, the foods that are required to prevent and treat some of the co-morbidities and how nutrient requirements can be achieved on such low energy intakes.

Is this the right room for an argument? - Behaviour as a form of communication

John Ford, Tautoko Services, New Zealand

Building relationships with people who have Prader-Willi Syndrome through an understanding of how the syndrome influences thinking, feeling and styles of information processing.

People who have Prader Willi Syndrome often seem to have particular patterns of cognitive abilities and disabilities in addition to their physical ones. In this session I'll reflect on some of the interactions that I have observed while supporting people who have PWS and those who care about them. We'll compare these observations with the research literature and draw some likely conclusions about the information processing styles of people who have PWS, and hence about the way that the social world may look to a person has the syndrome.
Our goal will be a deeper understanding of the reasons why people with PWS seem so often to be in conflict with those around them and why these conflicts often seem so intractable and unproductive. We'll conclude by looking at the tools that such an understanding might give us for communicating more effectively.

Medication in the Treatment of Behaviour and the Ethics of Food Control

Tony Holland, Professor and Head of The Learning Disability Research Group, University of Cambridge, UK

Medication in the treatment of behaviour and the ethics of food control in PWS
This workshop will have the following aims:

- To consider the different types of behavioural and psychiatric problems that frequently affect people with PWS, how they present and how an understanding of such problems informs intervention;
- To consider under what circumstances different treatment approaches for behavioural and psychiatric problems may be indicated and under what circumstances psychiatric medications might be of benefit;
- To consider the responsibilities that families and paid carers of children or adults with PWS have to prevent obesity and under what circumstances control of access to food is ethically and legally justified.

Those attending the workshop will be asked to draw upon their own direct experience supporting people with PWS and to bring their own examples to the workshop for discussion.

Prader-Willi Syndrome: Evidence Supporting an Autistic Spectrum

Merlin G. Butler, MD, PhD Kansas City School of Medicine, USA

Prader-Willi syndrome (PWS) is characterized by infantile hypotonia with feeding difficulties, hypogonadism, hyperphagia with early childhood obesity, small hands and feet and learning/behavior problems. PWS is generally due to a chromosome 15q11-q13 deletion of paternal origin but may also be due to maternal disomy 15. Prader-Willi syndrome and Angelman syndrome (AS), a clinically distinct sister syndrome generally due to a 15q11-q13 deletion of maternal origin or occasionally paternal disomy 15, are examples of genomic imprinting conditions whereby gene expression depends on the parent of origin. In addition, duplications within the 15q11-q13 region particularly of maternal origin have been associated with autism. On occasion, PWS subjects present with autistic features particularly those with maternal disomy 15.

Autism is not a single entity but consists of several causes with varying degrees of severity but several lines of evidence indicate that genetics plays a role. Abnormalities of chromosome 15 including duplications, deletions, or inversions of the 15q11-q13 region are the most frequently seen cytogenetic findings in autism and affects about 4% of autistic individuals. Thus, the 15q11-q13 region contains genetic information playing a role in autism in a reported subset of individuals. Additionally, the recognition of autistic features in individuals with PWS (and AS) and in other genomic imprinting syndromes such as Rett further supports these observations. To date, several candidate genes have been proposed for autism with reported involvement of over 20 genes including those on chromosome 15. Autism susceptibility genes in the 15q11-q13 region include UBE3A, a maternally expressed gene which causes Angelman syndrome and involved with brain development. Other potential genes of interest for autism found in the 15q11-q13 region include three GABA receptor genes (GABRB3, GABRA5, GABRG3) which are paternally biased in gene expression. GABA is a major brain chemical (an inhibitory neurotransmitter). Mice deficient for the GABA receptor beta 3 (GABRB3) gene present with epilepsy and learning deficits similarly seen in autistic individuals. In addition, plasma GABA levels are abnormal in subjects with PWS compared with controls and in autistic youngsters. The 15q11-q13 region also contains several small genetic (RNA) molecules known as non-coding RNAs. Non-coding RNAs do not code for protein but appear to play a role in controlling expression of genes they bind to and target. Recently, HBII-52 (a snoRNA in the 15q11-q13 region) was found to regulate a specific serotonin receptor (HRT2C) gene not located on chromosome 15. Serotonin related genes are also thought to play a role in autism. Thus, these genes as well as other genes in the chromosome 15q11-q13 region (when disturbed) lead to PWS and possibly to autistic features. Several features seen in individuals with PWS are

similarly seen in autistic persons such as superior skills for a narrow range of abilities with calendars, calculations, music or enhanced visual memory despite potential impaired cognition. During infancy, autistic children may be extremely passive and require little attention but may be irritable and difficult to feed or have irregular sleep patterns similarly seen in PWS infants. Repetitive behavior activities are consistently seen in autism and in some children with PWS. Thus, a greater insight into converging biological factors that cause autism may be gained by comparing autism to disorders with autistic features and relatively well-delineated genetic etiologies or with neurobiological findings as noted in PWS.

Understanding routines, repetitive questions and temper outbursts in Prader-Willi Syndrome

Chris Oliver, Kate Woodcock and Glyn Humphreys. Centre for Neurodevelopmental Disorders, School of Psychology, University of Birmingham, Birmingham UK.

Strong preference for routine, repetitive questioning and temper outbursts are prominent features of the behavioural phenotype of PWS for some children. We have used a variety of methods (clinical interview, cognitive assessment and behavioural challenges) to understand how compromised attentional shift might be related to each of these behaviours and the relationship between the behaviours. Using cognitive assessments we were able to demonstrate that compromised attentional shift was a feature of PWS and related to preference for routine and repetitive questioning. At interview parents report a sequence to these two behaviours and temper tantrums under specific environmental conditions and we were able to demonstrate this sequence empirically using observational methods. Finally, we challenged attentional shift in experimental and naturalistic settings and showed evidence that this was related to precursors to tantrums, such as increased questioning, facial expression and elevated variability in heart rate. The implications of these studies for the further delineation of PWS and intervention are discussed.

Schooling Options

Helen Anderson, PWSA of Victoria, Australia

What type of school
Local Primary, private school, primary school with integrated classes or special school? How can you tell which is the best for your child and who can you talk to about it.
The search for a school
When should you start looking. How much should you tell them about PWS. What should I be looking at - class size, state of the art equipment etc.
The perfect school (or the best option) and extra help for your child
Depending on the type of school you've chosen - does the school need to seek funding for extra help. What will help that process. What to do if you are not successful with funding.
Getting your child ready for school and the school ready for your child
What do you need to tell the school about your child and what do you need to tell them about PWS. What documentation do you need to provide. What will help to settle them into their new routine.
At school
What needs to be in place to ensure that your child has a successful start at school. How much do you need to tell other parents and/or students. How you can help.
If it all goes pear shaped
What to do next, who to consult.

Some Reflections on Developments in Residential Services for People with Prader Willi Syndrome

Angus Capie, Clinical Psychologist, Standards & Monitoring Board, Wellington, New Zealand

The identification of Prader Willi syndrome in 1956 occurred at the same time that some major re- thinking was occurring about the place in society of people with disabilities, and how their residential needs could best be met . Looking back over fifty years we have to ask

- "What should we have done differently?
- "Are we continuing to make the same mistakes?"

This paper reviews some of the changes that have taken place in residential service models, and looks at some of the service models developed internationally for people with PWS. .It asks

- "Are residential services designed to meet the needs of the services users or are they designed to suit service providers?
- How can we ensure that people with PWS are supported to lead individual lives of quality?
- Do residential services focus on the syndrome rather than the individual?
- It will conclude with some guidelines on how to achieve quality services

Service Delivery Strategies that Promote Quality of Life for Individuals with Prader-Willi Syndrome

Anna Hughes, Leveda Inc. 2 Peaton Avenue, Ingle Farm, South Australia 5098,

The issue of quality of life for someone with Prader-Willi Syndrome is an ongoing one. As a society we value our liberty. People with Prader-Willi Syndrome have the same aspirations of freedom and right to choice. Without life however, there is no freedom and no ability to choose. Prader-Willi Syndrome is a life threatening disorder. In order to achieve quality of life, the right to life must be upheld primarily. The nature of the syndrome and its implications must be considered foremost in order to achieve quality of life.

Leveda is an accommodation and community support service for people with disabilities and complex support needs; providing services to people in the North and North Eastern suburbs of Adelaide in South Australia.

In 2002 Leveda was successful in gaining the tender to provide services specifically for individuals with Prader-Willi Syndrome and associated disorders.
In October of 2002 a group of four individuals with Prader-Willi Syndrome and one individual with an associated disorder transitioned to a group home specifically designed to meet the needs of this client group. At the time this was only the second such accommodation service of its kind in Australia. The service at Leveda has been operational for over 5 years and during this time parents, support workers and the clients themselves have worked hard at finding the balance between the management of the syndrome and the ability to achieve the highest quality of life. During this time due to the effective implementation of service delivery strategies the clients have been supported to achieve the highest possible quality of life. Clients' weights have been able to be maintained within 15 kilograms of their healthy weight range with many clients being within their healthy weight range most of the time. Clients enjoy a full social life including going out for dinner on a regular basis. All clients attend either school, day placement, or work and issues in these areas are managed efficiently with supporting service delivery strategies. Two clients have transitioned to an environment that enables more independent living without

compromising the support needs that their disability requires and have achieved what they view as greater independence, more freedom and a better quality of life. Two more clients have transitioned to the original service and have maintained their weights within the healthy weight range. Leveda has explored options that will better meet the needs of individuals currently residing at this service and have submitted plans for a new dwelling. It is hoped that the design of the new dwelling will enhance quality of life for the individuals we support.

There is no doubt that achieving quality of life for people with Prader-Willi Syndrome will remain a challenge particularly in a society where food is a major focus of our social events and interactions. There is no line over which this client group can step and leave their syndrome behind to achieve quality of life without threat to life. This presentation will demonstrate that when service delivery strategies and supports focus on the nature of the disability and its implications individuals are able to achieve quality of life in harmony with their disability.

Poster Presentations - Abstracts

Poster Board #1

Parent Training for Prader-Willi Syndrome

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Introduction: This study examined the effects of parent training on the parenting style of parents of children with Prader-Willi Syndrome (PWS). This program was based on cognitive behavior therapy (CBT), especially on functional assessment-based behavioral interventions on the child's behaviors by parent.
Method: Participants in this program were eleven parents, eight mothers and tree fathers from eight families. Six sessions were held every two weeks. Each session, with the exception of the first, began with a review of the previous session, including homework. This was followed by the lectures about some methods of behavior modification. Parents then broke into three groups by children's age to complete group works about the lectures, and determined their child's target behavior to record the frequencies as homework. Mothers and fathers from the same family were assigned to the same group. We positioned second 2-weeks interval as baseline term, third as first intervention term, forth as second one and fifth as third one. Especially, in the first intervention term, the intervention procedure proposed to participants was only to praise appropriate behaviors of their child. In the second and third intervention they could add some other procedures such as differential reinforcement, environmental adjustment or token economy system along their purposes. Participants used problem-resolving method to determine which procedures were the most effective for their child or easy to execute for them. To measure parental anxiety, State Form(STAI-S) of State and Trait Anxiety Inventory (STAI) was used.
Results: In four children (four families) among eight children, the frequencies of their targeted maladaptive behavior decreased or disappeared in the first intervention term. So their parents chose a new target behavior and added some procedures effectively. In another child, a targeted appropriate behavior was shaped in the first intervention term. But in this term some parents used other procedures than praising. In other two children, the target behavior of each child was finally improved, too. In the other child, the target behavior was too difficult to decrease adequately. At six months' following-up, it was confirmed that the effects about the target behaviors had been maintained in children of 7 families. The STAI-S average score of the parents (n=7) who took part in all sessions tended to decrease from pre (session1, 51.2) to post (session6, 39.7).
Conclusion: It was suggested that CBT based parent training is effective for parents of child with PWS as same as parents of their child with ADHD or Mental Retardation. But at six months' following-up, it appeared that some parents couldn't have confidence in trying again without helping professionals when they faced new problems. We should pay more attention to make continuous supporting systems from now on.

Poster Board #2

Anna Hughes, Levada Inc. Residential Services

Poster Board #3

"Addressing the balance"

Authors : Francie Thornton – young woman living with Prader Willi Syndrome accessing residential and vocational Services provided by Idea Services

Patricia Matthews- Behaviour Support Worker for Idea Services

Main Themes: This poster looks at the issue of balance with regards to an individual young woman's rights to freedom of choice and expression versus a young woman with Prader-Willi Syndrome's need to have certain freedoms curtailed; and an employee's right to expect to be treated with respect in the workplace versus the sometimes inevitable behavioural consequences of the frustrations of living with PWS.

Poster Board #4

Hohepa Residential Services

Poster Board #5

Medical Clinics for Adolescents & Adults with Prader-Willi Syndrome

Georgina Loughnan, Janet Franklin, Elisia Manson, Kate Steinbeck, MD
Metabolism & Obesity Services, Endocrinology Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia. Tel: 61 2 95154230 Fax: 61 2 95155820 Email: georgie@email.cs.nsw.gov.au

Early diagnosis of neonates with Prader-Willi Syndrome (PWS) is now the norm rather than the exception. Medical management is commenced at an early age and follow up is often continued through a paediatric hospital endocrine clinic where physical therapy, speech therapy and occupational therapy are routinely provided. In Australia children with PWS can access clinics in most capital cities. To date, there are only two clinics for adolescents and adults with PWS. Australia's land size is 7,659,861 square metres! As several clients who attended the nearby children's hospital were aged over 25 years, our clinic for obesity management at a major public adult teaching hospital was approached in 1991 to take on the care of adults with PWS. More people with PWS were living longer and a need was seen for an adult clinic. Metabolism & Obesity Services (MOS) decided to trial such a clinic and assess its viability. Our PWS Clinic has now been operating for the past 17 years and has seen 61 genetically diagnosed clients with PWS. The clinic aims to promote optimum health, weight management and appropriate environmental care for adolescents and adults with PWS. PWS protocols have been initiated to be used for client hospital admission. Established links with other hospital services has resulted in prioritised treatment for PWS clients. This clinic is involved in ongoing research, education, support and advocacy for clients with PWS both clinically and in the wider community.

Poster Board #6 & #7

Special Residential Schools

Salisbury School for Girls, Nelson and Halswell School in Christchurch. Both schools are special residential schools which have shown great success in the care and education of girls and boys with PWS

Speaker Biographies

Helen Anderson
Organising Committee
email: haa@optusnet.com.au
Helen is a graphic/web designer and the mother of Natalie, aged 16 who has PWS. She is married to Bryce and also has a son, Jeremy, who is 13 years old. Helen was one of the founding members of the Australian PWS Association and is a committee member of the Victorian Association. She is responsible for the websites of both Associations and the design and artwork of this conference and is on the organizing committee.

Merlin Butler
email*:* mgbutler@cmh.edu
Chief of the Section of Medical Genetics and Molecular Medicine at Children's Mercy Hospitals and Clinics, Chair in Medical Genetics, and Professor of Pediatrics at the University of Missouri, Kansas City School of Medicine.
Professor Butler is Chairperson of the Scientific Advisory Board of the PWSA (USA) and has carried out genetics research on PWS, Angelman's Syndrome, Fragile X Syndrome, autism and obesity. He is the author of over 300 research articles. He was recently listed in the 2004-5 Guide to America's Top Physicians by the Consumer's Research Council of America. He is an editor of two textbooks: *Management of Prader-Willi Syndrome*, 3rd edition., Springer Verlag NY, and *Genetics of Developmental Disabilities*, 1st edition, Taylor & Francis Publishers.

Angus Capie
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Angus Capie trained as a clinical psychologist and has worked with people with disabilities and their families for most of his working life. During that time he has have been involved in assessment/treatment programmes, in developing new models of residential and day services, and in training staff at all levels.
For the last twenty years, his focus has been on working with service users, families and providers to enhance the quality of life offered through service development and evaluation. He has taught in Australasia and the Pacific Islands, Europe and North America,. In 2006 he was made a Fellow of the Australasian Society for the Study of Intellectual Disability .Angus has written several books. His interest in Prader Willi Syndrome was aroused when he became aware of the real challenges faced by families and providers in meeting the needs of young people with PWS. Angus is currently on the Board of the NZ PWS Association.

Patricia Crock
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Paediatric Endocrinologist based at the John Hunter Children's Hospital in Newcastle, New South Wales.
Tricia trained at the Montreal Children's Hospital and McGill University, Montreal, Quebec, Canada and at the Astrid Lindgren Childrens' Hospital, and Karolinska Institute, Stockholm, Sweden with Professor Martin Ritzen who has had a long standing interest in Prader Willi syndrome. Tricia has a particular interest in congenital pituitary and hypothalamic disorders and is a paediatric advisor on the board of the Pituitary Network Association in the USA. As Past-President of APEG (Australasian Paediatric Endocrine Group), she has been actively involved in advocating for growth hormone therapy for children with PWS in Australia.

Peter Davies
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Director of Research, School of Medicine, Director, Children's Nutrition Research Centre, Discipline of Paediatrics and Child Health, University of Queensland, Royal Children's Hospital. Brisbane. Telephone +62.7.3636 3765
Associate Professor Davies has had a long-term interest in PWS and has published a number of papers relating to energy metabolism, body composition and growth hormone treatment in the syndrome in the international literature. Much of Peter's work has utilised isotopic tracers to investigate body composition and energy metabolism in health and disease. The Children's Nutrition Research Centre, in Brisbane, that Peter leads has a significant research focus in paediatric growth and development including children with PWS. Peter is the National Chair of Nutrition Australia and is scientific adviser to the Australian and New Zealand PWS Associations.

Urs Eiholzer
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Associate Professor, University of Zurich, head of 'Centre for Pediatric Endocrinology, Zurich, Switzerland
Urs Eiholzer, MD, is a pediatric endocrinologist with additional training in psychosocial and psychosomatic medicine. He is Associate Professor at the University of Zurich and head of the Centre for Pediatric Endocrinology, Zurich. He was a fellow of Professor Andrea Prader [*of Prader-Willi Syndrome*] and Professor Milo Zachmann and has published extensively on various aspects of somatic growth, pubertal and psychomotor development and regulation of appetite, physical activity and body composition in PWS. He is the author of scientific publications and several books addressing patients and their families.

Pam Eisen
email*:* pame.1@comcast.net
President, International Prader-Willi Syndrome Organisation (IPWSO)2004 – 2008
Pam is the mother of Gabriella, 27 years old, with PWS and two sons, Jeremy and Benjy. She has a B.S. in Child Development and Graduate Studies in Psychology. Pam is in her second term of Presidency, and is responsible for the overall guidance of the International PWS Organisation. Her busy schedule has her involved with establishing and forming new PW Associations in emerging countries, networking with governments and health agencies, attending international paediatric and medical conferences throughout the world promoting the work of IPWSO. Pam is currently involved in the first Caregivers Conference to be held in June in Germany this year the outcome of which will give an overarching guidance for PWS residential care.

John Ford
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John Ford is a registered psychologist who specialises in support to people who have intellectual disabilities and the kind of behaviour that we euphemistically refer to as 'challenging'. John is lucky enough to be married to Christine and over the past 20 years the two of them have enjoyed supporting a number of people, both children and adults, who have PWS. John and Christine are employed by Tautoko Services and are based in Nelson.

Janet Franklin
email: frank@email.cs.nsw.gov.au
Janet Franklin is a senior dietician at Metabolism and Obesity Services Royal Prince Albert hospital and the primary dietician for the RPAH PWS Clinic. She is currently completing a PhD

into childhood obesity and its associations with self perception, self esteem, victimisation and lifestyle factors. She founded and continues to chair the DAA National Obesity Interest Group and is a Member of the "The Obesity Society" (formally ASSO). As well as overseeing the nutrition plans of the PWS clients she coordinates their clinic activity sessions.

Barry Greensmith
Conference Co-host
email: northstateage@optusnet.com.au
Barry is married to Maureen and is the father to James who is 18years old and has PWS. They reside in Newcastle, New South Wales, Australia. Barry has his own business and is the current President of the Prader-Willi Syndrome Association of Australia and Co-Chair of this Conference

Tomoko Hasegawa
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Clinical geneticist and pediatrician. Educated in medicine in Japan. Studied clinical genetics and cytogenetics in Germany as an assistant doctor (1973 –1975). Chief of the Clinical Genetics and Cytogenetics Division of Shizuoka Children's Hospital, Japan (1985 – 2003) and started PWS Clinic in 1996. Analyzed chromosomes from many individuals with PWS. In 2005 set up Genetic Support and Consultation Office. Attended International PWS Conferences since the first in 1991. Cooperated with the parents for organizing PWSA Japan in 2005. Professional Delegate for IPWSO.

Paul Hofman
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President of the New Zealand PWS Society; Clinical Director of Paediatric Endocrinology and Diabetes at the Starship Children's Hospital, Auckland; Associate Professor, Liggins Institute, University of Auckland.
Paul is a paediatric endocrinologist and has research interests including insulin sensitivity, the metabolic syndrome and growth. He is the current treasurer of the Australasian Paediatric Endocrine Group (APEG) and is involved on APEG committees including review of PWS respiratory monitoring and congenital adrenal hyperplasia. He has a particular clinical interest in, and active involvement with children and adolescents with PWS. As a member of the New Zealand Growth Hormone committee he has been actively involved in promoting growth hormone therapy for PWS.

Tony Holland
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Developmental Psychology Section, University of Cambridge, CB2 2AH, President of the PWSA (UK)
Professor Holland is the Head of The Learning Disability Research Group at the University of Cambridge Department of Psychiatry. His work includes investigation into satiety, mood disorder and psychiatric illnesses associated with PWS. He is also President of the PWS Association (UK) and his recent work has included investigating the very early phenotype of PWS and characterising when the eating problems first emerge, using brain-scanning techniques to investigate satiety. His interest lies in characterising the psychiatric illnesses associated with PWS. Tony has spoken at all IPWSO (International PWS Organisation) conferences since their inception in 1989 and been on the organising committee for the Scientific programmes.

Charlotte Hoybye
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Department of Endocrinology, Metabolism and Diabetes, Karolinska University Hospital, Solna, 171 76 Stockholm, Sweden
Doctor Hoybye gained her MD in 1986 from Aarhus University, Denmark. She specialised in internal medicine in 1993 and in endocrinology in 1996. In 2003 Charlotte gained her PhD from the Karolinska Institute, Stockholm, Sweden. The topic of her thesis was "Endocrine and Metabolic Aspects of Adult Prader-Willi Syndrome with Special Emphasis on the Effect of Growth Hormone Treatment". Since 2001 she has been a consultant in endocrinology and internal medicine at the Department of Endocrinology and Diabetes, Karolinska Hospital, Stockholm, Sweden and since 1997 has worked clinically and scientifically with PWS patients.

Anna Hughes
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Program Manager, Leveda Inc. Supported Accommodation and Community Support Services, 2 Peaton Ave Ingle Farm South Australia.
Anna has worked in the disability sector for 9 years and has a daughter with a disability. Anna completed certificate 3 and 4 in Disability Studies and is currently in her 3rd year of the degree in Disability and Community Rehabilitation. She was responsible for the management of a service specifically set up for people with Prader-Willi Syndrome and associated disorders within the Leveda Supported Accommodation Services in South Australia (the second only service of its kind in Australia at the time from 2002 to 2005.) Anna developed service delivery strategies to support quality of life for these individuals which include delivering training in the area of PWS and nutrition both organizationally and in the community.

Shuan-Pei Lin
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Director of Division of Genetics and Metabolism, Departments of Pediatrics and Medical Research, Mackay Memorial Hospital, Taipei, Taiwan, Vice-President of IPWSO
Assistant Professor of Department of Infant and Child Care, National Taipei College of Nursing, and Department of Early Childhood Care and Education, Mackay Medicine, Nursing and Management College, Taipei, Taiwan. Board Member of IPWSO, Taiwan Human Genetics Society, Taiwan Pediatric Association, Down Syndrome Foundation of ROC, and Taiwan Foundation for Rare Disorders. Committee Member of Deliberation Committee for Rare Diseases and Orphan Drugs, Department of Health, Taiwan, Committee of Promotion for Early Intervention, Taipei City Government, Taiwan, Committee of Continuous Medical Education, Taipei Medical Association, Taiwan, Committee of Early Intervention for Disabled Children, Mackay Memorial Hospital, Taipei, Taiwan. Medical Consultant of PWSA-Taiwan, Taiwan MPS Society, Taiwan OI Association, Taiwan Albinism Association, and Taipei Disability Swimming Associations

Georgina Loughnan
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Metabolism & Obesity Services, Endocrinology Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia.
Georgina has been a clinician at Metabolism and Obesity Services for the past 25 years. Her role is to counsel obese people in exercise, nutrition and cognitive management of their weight problem. She now specialises in seeing clients with intellectual disabilities or mental illness. In 1991 she commenced a clinic for adults with PWS in Sydney. The clinic gradually expanded to see adolescents and adults with PWS, who are now seen on a regular basis for ongoing medical care and weight loss management and support The multi-disciplinary clinic includes

the services of a dietician, physiotherapists social workers and endocrinologists. The clinic provides support and training in PWS to carers and other relevant people in the client's life. 62 clients diagnosed with PWS have been seen over the past 17 years. Georgina has presented at several IPWSO Conferences, Australasian PWS Conferences and Obesity Conferences. She has participated on several organising committees.

Nobuyuki Murakami
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Pediatrician, Department of Pediatrics, Kochi Medical School:
May,1986- March, 1991 Resident and Senior Resident, Department of Child Neurology, National Center Hospital for Neuromuscular and Psychiatry Disorders (NCNP): April, 1991-September, 1996 Research fellow: Department of Anatomy & Structural Biology, Otago School of Medical Sciences, New Zealand: October, 1996-September, 1998 Pediatrician, Department of Pediatrics, Dokkyo Medical University, Koshigaya Hospital, Japan: October, 1998-onward

Toshiro Nagai
Toshiro Nagai, M.D., Ph.D. Dr Nagai studied medicine at the Kobe University, School of Medicine in April 1974. He is currently the President of the Japan Society of Pediatric Genetics and Professor and Director of the Department of Pediatrics, Dokkyo Medical University, Koshigaya Hospital, and Director, Department of Pediatrics, Tokyo Metropolitan Kiyose Children's Hospital.

Chris Oliver
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Chris Oliver, BSc, MPhil, PhD, AFBPsS, CPsychol, Professor of Clinical Psychology at the University of Birmingham UK.
Chris trained as a clinical psychologist at Edinburgh University before completing a PhD on self-injurious behaviour in people with intellectual disability at the Institute of Psychiatry, London. He has also researched behaviour disorders in people with severe intellectual disability and gene-behaviour associations. His current research interests include behaviour, cognitive and emotional disorders in people who have PWS, Fragile X, Cri du Chat, Lowe, Angelman, Smith-Magenis and Cornelia de Lange Syndromes.

Arabella (Ellie) Smith
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Senior Staff Specialist, Associate Head Dept of Cytogenetics, Children's Hospital at Westmead, Hawkesbury Rd, Westmead 2145, Australia.
Graduation at the University of Sydney (MB BS Hons II) was followed by a period of part time work at the Oliver Latham Laboratory NSW Dept of Health, involving newborn screening programmes and from 1979, cytogenetics. Post-graduate qualifications were obtained in the UK in 1988 with the Diploma in Clinical Cytogenetics and Molecular Genetics (DipRCPath), Human Genetics Society of Australasia Certification in Clinical Cytogenetics in 1989 (FHGSA) and the Royal College of Pathologists, Australasia in 1990 (FRCPA). PWS has been a major research interest since 1979 with several grants including two 5-year NH & MRC grants to do with PWS and Angelman Syndrome. Ellie has over 100 original publications in reputable medical journals with 30 relating to PWS and AS. In 2007 Ellie was awarded an IPWSO recognition and appreciation award for work done in advancing PWS knowledge.

Warwick Smith
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Dr Warwick Smith MBChB FRACP, General and Developmental Paediatrician at Kidz First at Middlemore Hospital, Auckland
Warwick is in private practice. His interests include autism, ADHD, complex neuro-developmental disability and the health-education interface. He attended the 4th International PWS Conference in Romania in June, 2007 which has increased his interest in PWS.

Kate Steinbeck
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Senior Staff Specialist in Endocrinology and Adolescent Medicine at Royal Prince Alfred Hospital, Sydney.
Kate holds a clinical academic position at the University of Sydney as Associate Professor. She is Director of the Metabolism and Obesity Services at Royal Prince Alfred Hospital and as part of this service established the Adult and Adolescent Prader-Willi Service in 1983 and the Family Weight Management Clinic. Her clinical interests include childhood and adolescent obesity (including the management of adolescent an adult patients with PWS) adolescent endocrinology and the impact of chronic illness on growth and development in adolescents. The Adult and Adolescent PWS service acts as a state-wide resource with Georgina Loughnan as Clinic Coordinator. Kate has written a book, "Growing Up, Not Out – a weight management guide for families" a book for families and the community.

Linda Thornton
Conference Co-host
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Linda is the National Director and founder of the PWS Association, New Zealand. She is editor of the Australasian newsletter, "PWS Downunder" and the IPWSO newsletter, "Wavelength". She is a founder member of the International PWS Organisation and has been re-elected to its Board as Secretary. Linda was on the organising committee of the 4th International PWS Conference and co-host of the 5th 2004 International PWS Conference. In 1999 she was awarded a Churchill Fellowship to study residential living for those with PWS and travelled to UK and USA, her study culminating in new guidelines for residential care in New Zealand. She was awarded the Queen's Service Medal for services to the community in 1999 and in 2007 received an IPWSO award as an exceptional contributor.

Alex Viardot
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Dr Alexander Viardot, Endocrinologist, FRACP.
Alex is originally from Basel, Switzerland, where he completed his medical training in internal medicine and endocrinology, and he moved to Australia four years ago to start his research at the Garvan Institute of Medical Research in Sydney within the Diabetes & Obesity Research Program. He is finishing his PhD this year under the supervision of Prof Lesley Campbell, his main research interests being appetite regulating hormones and inflammatory markers in PWS, type 2 diabetes and pre-diabetes.

Brendon Yee
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Consultant Physician, Respiratory and Sleep Medicine. Acting Head, Clinical Sleep Services;Department of Respiratory and Sleep Medicine;Royal Prince Alfred Hospital, Sydney
Brendon obtained his undergraduate medical degree from the University of Otago. He then obtained his specialist training in Respiratory and Sleep Medicine in Wellington. Brendon then

obtained his PhD (University of Sydney), “Aspects of treating obesity and Obstructive Sleep Apnea”. He is currently working as a Staff Physician at the Royal Prince Alfred Hospital and a Clinical Senior Lecturer (University of Sydney) Brendon has an interest in the interaction of obesity, metabolism and obstructive sleep apnea.

ADDENDUM
FUTURE RESEARCH IN PWS

One of the most important issues that we as parents and professionals, should be continually looking towards is the research that is being done in the PWS world that allows us to understand the how’s why’s and wherefores of the syndrome. Much research is done by examining the brain of a deceased person – perhaps a subject that as parents and caregivers we don’t like to think about. But this work is vital and donations of this extreme nature are rare and valuable. We had occasion in New Zealand to be able to send the brain of a baby with PWS who died a cot-death, to Holland were Professor Dick Swaab’s laboratory was able to examine it. We also had occasion to draw Professor Swaab’s attention to the question of whether the ageing process in PWS could possibly include Alzheimers Disease. He was intrigued with this question and reported back to us:

> “Following your suggestion up with stainings for hyperphosphorylated tau and a silver staining (Bodian), we found indeed evidence for a premature occurrence of AD in PWS. A remarkable finding was the pronounced early Alzheimer’s change (hyperphosphorylated tau) found in the hypothalamus, which is not observed in sporadic AD patients. However, more brain material of PWS patients over the age of 49 is urgently needed to see whether premature Alzheimer changes indeed occur in PWS. There is contact with the PWS Brain Bank in Florida, but it appears to be extremely difficult to get material from them to Europe. In addition the patients from whom they have material are well below 49 years of age.
>
> So we confirmed our earlier impression but cannot progress because of lack of postmortem brain material.”

This study was a “first” and came from parental observation of their mid-aged son which was able to be followed up by examination of brain tissue. Should you wish to consider further the possibility of contributing to this research, you may contact Professor Swaab:

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Professor Swaab has kindly submitted for reprint, his latest research in abstract form to include here in our Conference Programme.

THE HYPOTHALAMUS AND BRAIN BANKING IN PRADER WILLI SYNDROME

D.F. Swaab, Netherlands Institute for Neuroscience, Amsterdam, the Netherlands.

HYPOTHALAMIC SYSTEMS. Dysfunction of hypothalamic systems is the basis of most of the symptoms in PWS. The paraventricular nucleus (PVN) of the hypothalamus is a central structure for integration and regulation of e.g. eating, metabolism and autonomic processes. We found in post-mortem material that the volume of the PVN is 28% smaller and the total cell number is 38% lower in PWS patients. The number of oxytocin neurons – the putative satiety neurons – in the hypothalamic PVN is markedly decreased in PWS. This is a possible basis of the insatiable hunger and obesity of patients with the syndrome.

With A.P.Goldstone and U. Unmehopa we looked for a number of neuropeptide sytems that might be responsible for PWS symptoms. Short stature is accounted for partly by hypogonadism and partly by a growth hormone (GH) deficiency. However, growth hormone releasing hormone (GHRH) cell number in the hypothalamic arcuate or infundibular nucleus was found not to be reduced in PWS subjects. Neuropeptide Y (NPY) and agouti-related protein (AGRP) stimulate feeding. NPY staining and mRNA expression in the infundibular nucleus appeared, however, not to be increased but reduced in PWS and non-PWS obese subjects, compared to controls, while AGRP ICC staining was unchanged. These results show that the NPY/AGRP neurons are not defective and react normally on obesity in PWS. Although some PWS patients said to be cataplectic, we found (with R. Fronczek) no cell loss in the orexin/ hypocretin system in the lateral hypothalamus of PWS patients..

PWS REGION GENES are localized in human post-mortem material for validation and interpretation of the data obtained with transgenic mice and molecular genetic observations. The first pilot experiments are currently performed on C15 (with B.Horsthemke) and Necdin (with F. Muscatelli).

PREMATURE AGING IN PWS is studied at the suggestion of parents of patients. The first results confirm this possibility, with the most pronounced early Alzheimer's changes (hyperphosphorylated tau) found in the PWS hypothalamus, which is different from Alzheimer's disease.

BRAIN BANKING. Postmortem brain material of PWS patients is very difficult to obtain. We received the last 20 years only 16 PWS brains from 8 countries. This type of studies is further complicated by a large number of confounders that may influence observations on the hypothalamus. Antemortem factors (age, sex, medicines, seasonal and circadian variations and lateralization), factors during dying (prolonged illness, agonal state) and postmortem factors (postmortem delay, storage) all play a role. Therefore a large number of controls to match is needed for each study. Since the establishment of the Netherlands Brain Bank in 1985, we collected some 2,000 formalin fixed paraffin embedded serially sectioned hypothalami that are used for this purpose. More brain material of PWS patients is, however, urgently needed for different lines of research. Suggestions to improve the procedures for PWS brain donation are very much welcomed.