

OZGROW Report 2009/2010

GH therapy in Australia

As of May 2010 there are 1636 children receiving GH treatment in Australia under the PBS. The Department of Health and Ageing's (DoHA) indication for GH treatment of "Slow Growing", which incorporates idiopathic short stature, continues to account for most GH prescriptions with 818 children or 50% of the total. "Biochemical" GH deficiency (344, 21%), Turner Syndrome (224, 13.7%), Prader Willi Syndrome (88, 5.4%) being the other major categories. Other indications such as Cranial Tumour/Irradiation (69, 4.2%), Chronic Renal Failure (58, 3.5%), Hypoglycaemia (34, 2.1%), and Precocious Puberty (1) were also represented. The relative changes in total numbers of children prescribed GH and the breakdown across DoHA indications over the last three years is shown in Table 1 below.

Table 1. Patients Receiving GH for Each DoHA Indication Over Previous Three Years.

Indication	16/01/2008	31/01/2009	31/01/2010	28/02/2010
Slow Growing	851 (55.3%)	903 (53.2%)	982 (51.6%)	858 (51.3%)
Biochemical GHD	272 (17.7%)	307 (18.1%)	386 (20.3%)	348 (20.8%)
Cranial Irradiation	84 (5.5%)	74 (4.4%)	98 (5.1%)	72 (4.3%)
Hypoglycaemia	51 (3.3%)	79 (4.7%)	33 (1.7%)	32 (1.9%)
Turner Syndrome	225 (14.6%)	277 (16.3%)	255 (13.4%)	229 (13.7%)
Chronic Renal Failure	55 (3.6%)	56 (3.3%)	77 (4.0%)	62 (3.7%)
Precocious Puberty	2 (0.0%)	2 (0.0%)	2 (0.0%)	2 (0.0%)
Prader-Willi Syndrome			70 (3.7%)	70 (4.2%)
Total	1540	1698	1903	1673

Table 1 also shows a dramatic drop in total patients receiving GH between January and February 2010. This occurred after an audit of the data by DoHA and followed the observation by OZGROW to DoHA that a number of patients who had not received GH for a number of years had not been officially designated as "Ceased" treatment by DoHA. A similar, but smaller adjusting audit also occurred in April 2010.

In 2009 patients with Prader Willi Syndrome (PWS) became eligible to receive GH under the Australian Government's PBS. Some individuals were retrospectively categorized under the DoHA Indication of PWS as early as February 2009. In April 2009 19 PWS patients were receiving GH and this number has steadily increased to the current 88 making it the fourth most common DoHA indication for GH.

Adverse Events related to GH therapy 2009/2010 reported to OZGROW

Only two adverse events were reported to OZGROW in this period. The first was the recurrence of a craniopharyngioma and the second the development of an osteochondroma. It should be noted that it is an important function of OZGROW to monitor adverse events in relation to the use of GH. However, this function is dependent upon the diligence of GH prescribers to report adverse events either directly to OZGROW or, preferably, through the Growth and Treatment Record that is submitted to DoHA. Minor adverse events

should be reported, as when compiled from the whole population may allow statistical analyses leading to important interpretations.

A similar situation exists with respect to the use of concomitant drugs, for example oestrogen in Turner Syndrome, as such information can prove invaluable in current and future audit that ultimately can lead to better treatment strategies. One piece of data that is of particular importance is Final Adult Height. The new Growth and Treatment Record has a box to enter this important datum.

Working With DoHA: The OZGROW and GETS Databases

Over the 2009-2010 periods OZGROW has worked closely with the Department of Health and Ageing (DoHA) on a number of issues. Primarily among these was DoHa's transition from its previous Paradox database to the new GETS database. In designing the new database OZGROW worked with DoHA to include fields that were important with respect to clinical and research use for APEG members. Second to this a protocol was devised to allow the OZGROW relevant data to be extracted from the GETS database and imported into OZGROW. An agreement was reached between OZGROW and DoHA for this extraction and transfer to occur quarterly. The extraction and transfer protocol has now been used successfully on three occasions. OZGROW is continuing to liaise with DoHA to fine tune and improve the data being transferred.

One specific area in which OZGROW has worked with DoHA was in the information to be collected with respect to the Prader Willi patients. A new form was designed for Pader Willi patients to fill in and a new table for that data incorporated into the GETS and OZGROW databases.

International Conferences

OZGROW Research Fellow Dr Ian Hughes presented two posters (see below) and represented APEG at the LWPES/ESPE Joint Meeting in New York in September 2009. Registration, accommodation, and flights were funded by the Children's nutrition Research Centre, The University of Queensland. Dr Hughes also presented two posters (see below) and represented APEG at the US Endo 2010 Conference in San Diego in June 2010. Registration, accommodation, flights, and abstract submission were funded jointly by Pfizer, Novo Nordisk, and The Department of Paediatric Endocrinology and Diabetes, Mater Children's Hospital.

Papers, Reports and Abstracts

The following papers have been published.

Hughes IP, Choong CS, Cotterill A, Harris M, Davies PS. Gender Bias in Children Receiving Growth Hormone Treatment. (2010).

J Clin Endocrinol Metab. **95**(3):1191-1198

Nyunt, O., Harris, M., Hughes, I., Huynh, T., Davies, PSW, AM Cotterill, AM

Benefit Of Early Commencement Of Growth Hormone Therapy In Children With Prader Willi Syndrome (2009). *Journal of Pediatric Endocrinology and Metabolism* **22**(12):1151-8.

Nambiar, S., Hughes, I., Davies, P.S.W

Developing waist-to-height ratio cut-offs to define overweight and obesity in children and adolescents. (2010) *Public Health Nutrition* Jan 26:1-9 [Epub ahead of print]

The following papers are have been submitted and are current under review.

Hughes, IP, Choong, CS, Cotterill, A, Harris, M, Davies PSW on behalf of the Australasian Paediatric Endocrine Group (APEG). The Influence of Secular Trend for Height on Eligibility for Growth Hormone Treatment.

Hughes, IP, Harris, M, Choong, CS, Ambler, GR, Cutfield, WS, Hofman, PL, Cowell, CT, Werther, G, Cotterill, A, Davies PSW on behalf of the Australasian Paediatric Endocrine Group (APEG).

Growth Hormone Treatment in Australia with International Comparisons: First Year Response for Growth Hormone Deficiency and Idiopathic Short Stature.

Hughes, IP, Choong, CS, Harris, M, Ambler, GR, Cutfield, WS, Hofman, PL, Cowell, CT, Werther, G, Cotterill, A, Davies PSW on behalf of the Australasian Paediatric Endocrine Group (APEG).

Younger Age and Increased Dose Interact to Improve Growth Hormone Response in Turner Syndrome: Australian Experience. (Submitted JCEM).

The following abstracts have been published.

Hughes, I.P., Choong, C., Cotterill, A.M., Harris, M., Davies, P.S.W. (2009). Gender bias in children receiving growth hormone treatment in Australia: No evidence of an ascertainment bias, Abstract P02-148. *Hormone Research* **72**:S3 253. LWPES/ESPE 8th Joint Meeting Global Care in Pediatrics Endocrinology. New York.

Hughes, I.P., Choong, C., Cotterill, A.M., Harris, M., Davies, P.S.W. (2009). GH treated children: difference in age at first presentation between boys and girls". Abstract P02-149. *Hormone Research* **72**:S3 253-4. LWPES/ESPE 8th Joint Meeting Global Care in Pediatrics Endocrinology. New York.

Hughes, IP, Choong, CS, Cotterill, A, Harris, M, Davies PSW
P2-359: Growth Hormone Treatment in Australia: Historical Trends and Demographics (OZGROW). *Endo 2010*. San Diego, June 19-22, 2010.

Hughes, IP, Choong, CS, Cotterill, A, Harris, M, Ambler, GR, Cutfield, WS, Hofman, PL, Cowell, CT, Werther, G, Davies PSW
P1-687:1st and 2nd Year Response to Growth Hormone Treatment for Turner Syndrome in Australia (OZGROW). *Endo 2010*. San Diego, June 19-22, 2010.

The following book review was requested and is published.

Hughes, I.

Pediatric Endocrinology and Inborn Errors of Metabolism (Book Review) (2009). *Journal of Paediatrics and Child Health* **45**(11) 668-669.

The following report was commissioned by APEG.

Hughes, I, and Choong, C

OZGROW Report for APEG, DoHA, PBAC Meeting of 08/04/2010 Regarding Amendments to the "Guidelines for the Availability of Human Growth Hormone as a Pharmaceutical Benefit". 1st April 2010.

OZGROW Collaborative Research Activity

1. Dr Elly Scheermeyre – Prader Willi Syndrome. Dr Scheermeyre was involved with OZGROW in determining fields to be used in the PWS specific table in the OZGROW and DoHA GETS databases. Access to the PWS relevant part of OZGROW database was granted to Dr Scheermeyre for her research once strict confidentiality protocols had been established.
2. Drs Steven McTaggart and Louise Conwell. GH use in renal transplant patients and a possible link to post transplant lymphoproliferative disease (PTLD). Dr Hughes linked the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) with OZGROW H numbers, while preserving patient confidentiality, to provide the researchers with GH treatment information in terms of renal identification numbers. A manuscript is in preparation.
3. Dr Justin Brown. Turner Syndrome. Assisted Dr Brown in preparation of his APEG Research Grant 2010 application.

OZGROW SubCommittee:

Members: Wayne Cutfield, George Werther, Chris Cowell, Catherine Choong

Chair: Catherine Choong

Ex officio: Ian Hughes, Peter Davies

The functions of OzGrow were ratified by the Ozgrow Subcommittee in the updated terms of reference as follows:

Role and Function of OZGROW

1. To maintain a de-identified registry (the OZGrow Database) of all Australian GH patients receiving GH as a Pharmaceutical Benefit
2. To maintain a de-identified registry of all New Zealand GH patients receiving GH as a Pharmaceutical Benefit
3. To record prospectively GH related diagnostic, treatment, and outcome data for all registrants until cessation of GH therapy

4. To collect, maintain and update the Ozgrow Database from de-identified data supplied by the Department of Health and Aging, Growth Centres and individual prescribers
5. To monitor efficacy and safety of GH therapy in Australasia
6. To provide support for the GHAC in its function as an independent panel of experienced paediatric endocrinologists appointed by The Australasian Paediatric Endocrine Group (APEG) to deliberate on cases which do not clearly fulfil the guidelines and where eligibility is uncertain, or where there is dispute about an eligibility decision.
7. To provide support for the relevant Officers within Department of Health and Aging in relation to the Pharmaceutical Benefit GH programme as directed by the Ozgrow Subcommittee
8. To provide relevant information to other institutional and commercial bodies as directed by the OzGrow Committee and APEG Council
9. To provide support and reports for the APEG council in relation to GH therapy and other relevant medical affairs
10. To provide support, data and reports for other APEG Registries as directed by APEG council including the Prader Willi Registry
11. To initiate, assist and facilitate research related to GH therapy and pediatric endocrinology

Funding and continued support of the APEG OzGrow database remains a major endeavour for the OzGrow Subcommittee. To date APEG has received yearly support for the Database and OzGrow activity from interested Pharmaceutical Bodies. The long term viability of the OzGrow Database is dependent on secure long term funding. This allows for planning and development and expansion of this resource which currently holds prospectively collected clinical information for all Commonwealth funded Growth Hormone Therapy since the early 1980's. The OzGrow Subcommittee is currently preparing a submission to the Department of Health of part support of this database.

The OzGrow Subcommittee is currently investigating the possibility of data linkage with other established databases and registries. This would enhance the capacity of the OzGrow Database considerably in relation to long term follow up of patients treated with Growth Hormone. This includes the National Cancer Registry and the other long term registries. In addition, we have discussed informally with our adult endocrine colleagues on the benefit and potential of extending the OzGrow Database to encompass Adult Growth Hormone Therapy in the event that Growth Hormone therapy for Adults receives approval for Commonwealth Funding in the future.

The OzGrow Subcommittee welcomes feedback and will be requesting nominations for the committee later in 2011.