



## Drug and Therapeutics Annual Report

### D&T Members 2009-2010:

- *Nicole Glaser, Catherine Gordon (Co-Chairs, 2009-2010)*
- *Constantin Polychronakos (CEG liaison), Sara Divall, Andrea Haqq, Stuart Weinzimer, Adda Grimberg, Steve Gitelman, Steven Waguespack, JB Quintos, Martin Draznin, Cem Demirci*
- *David Geller (Chair Emeritus)*
- *Ex-officio: Alan Rogol*

**General:** Alan will be completing his term as LWPES secretary in a few months. However, Alan reported that he will likely stay on the D +T in an advisory role. Alan has been a terrific resource for us and we look forward to continuing to work with him.

### Subcommittee Papers (works in progress):

1. ***“Use of Insulin Sensitizers in Adolescents with PCOS”***: David Geller (Chair), Madhu Misra, Daniele Pacaud

Manuscript was previously approved by the D&T, but was reviewed by the BOD last spring, with the recommendation to rewrite major portions. This subcommittee has agreed to work on the revision over the next few months.

The suggestion was made to put metformin in title as this agent is the only insulin sensitizer in use in pediatric clinical practice. Nicole and Catherine will contact David to find out how we can help him as a committee to make revisions and keep the manuscript moving forward. We will ask him to send the current draft to Committee to read again, and think about what revisions may be needed.

2. ***“Aspects of pediatric thyroid treatment” (effect of soy, pharmacy directives for taking l-T<sub>4</sub> on an empty stomach)***: Phil Zeitler & Paulo Collett-Solberg.

This manuscript is ready for submission and has been endorsed by LWPES. Phil was in communication with *Pediatrics* regarding publication but they did not recommend submission there because they felt it was not the right venue. Phil will try *J Peds* next. Searching for alternative journals if *J Peds* is not interested.

General discussion on submission of manuscripts that represent clinical reviews. We discussed whether there is a need for a cover letter for this type of submission from LWPES. Our thought was that this type of letter might facilitate the review process and increase interest in the work by a particular journal. Another example of this type of review is HHS manuscript. We discussed that many reports are of relevance to pediatricians. We thought that it is important to try to get interest from a particular journal long before submission of manuscripts.

3. ***“Hyperglycemic hyperosmolar states”***: Phil Zeitler (Chair), Nicole Glaser, Arlan Rosenbloom (Ad-hoc member), Andrea Haqq.

This manuscript is ready for submission and has received approval from LWPES BOD as endorsed guidelines. See #2 above regarding journal submission. *Pediatrics* had similar feelings about this manuscript as about the thyroid statement and stated that their journal was not the right audience – thought we should aim for more critical care oriented journal. We will plan on submitting to *J Pediatrics* and if not accepted there, will begin discussing other options .

4. ***“The use of bisphosphonates in children”***: Catherine Gordon (Chair); Leanne Ward (Co-chair and Ad-hoc member), Anna Petryk.

Recently published in *International Journal of Clinical Rheumatology*. Was initially sent to *Pediatrics* and was rejected.

5. ***“Use of statins in children with type 1 diabetes and hyperlipidemia”***: Nicole Glaser (Chair), David Geller, Andrea Haqq, Steve Gitelman and Mary Malloy (Ad-hoc member).

This manuscript has undergone initial review by D&T and has now been submitted for outside review. Once reviewed and revised, the manuscript will then be submitted for approval by BOD and then to a journal. A specific journal for submission has not yet been selected – the committee is considering *Diabetes Care*, *J Pediatrics* or *Pediatrics*. *Pediatric Diabetes* was also suggested. This manuscript will be a review, but will not represent official guidelines as the committee felt that available data are not sufficient to support one or another of the existing guidelines, nor are the data sufficient to generate new LWPES guidelines.

6. ***“Bariatric surgery in children”***: Andrea Haqq (chair), Leona Cutler (ad-hoc member), Tania Burgert (Yale, ad-hoc member), Michael. Helmuth (Bariatric Surgery at UNC, ad-hoc member), Michael Freemark (ad-hoc member, Duke).

Andrea updated us on the work of the subcommittee. The subcommittee represents an outstanding group of experts in this field. The group is working on an outline. The group will try to elicit interest from journals early on. *Obesity* was mentioned as a possibility. Many gaps in knowledge about this topic exist: defining these knowledge gaps will be the focus of the report.

7. Replacement manuscript ***“Guidelines for the use of growth hormone in children”***: Adda Grimberg (chair), Sara Divall, Constantin Polychronakos, JB Quintos.

As requested by the BOD, the older manuscript on the LWPES website was deemed to require updating, specifically in the following areas:

1. *New FDA-approved pediatric indications since then: SHOX haploinsufficiency, Noonan syndrome*
2. *Need for surveillance/treatment for central adrenal insufficiency.*
3. *PWS and sudden death info to be updated.*
4. *ISS: heterogeneous category: additional clinical studies, post-receptor GH/IGF axis defects identified.*
5. *Concept of primary IGF deficiency?*
6. *GH products, such as: Depot GH (once and future product), Combo GH/IGF-I in development, mention of IGF-I as therapeutic option and its indication?*
7. *GH and metabolic actions in children, citing pediatric studies.*

This document, like its predecessor, will take the form of a GUIDELINES type of paper, requiring substantial BOD involvement, in addition to their review of the document. The finished document would materially aid LWPES practitioners and would provide much-needed firepower for letters to insurers, etc. The BOD felt strongly that additional subcommittee members must have NO possible conflicts of interest/relations to pharmaceutical companies of any kind. Adda has begun to organize this subcommittee. Possible conflicts of interest are being reviewed by the BOD.

Alan reported that there are going to be new guidelines soon re: conflict of interest reporting within LWPES, and resolution thereof. A new conflict of interest disclosure form is also being created. Should have these guidelines within a month. Thereafter, Adda's candidates for the subcommittee will need to be evaluated carefully by the BOD, using these new criteria. Once her committee members have passed screening and are fully assembled, Adda will be able to begin work on the document.

8. ***“Use of RAI in Grave’s disease (GD in Grave’s Disease)”***: David Geller (Chair), Nicole Glaser, Daniele Pacaud, Scott Rivkees (*Ad-hoc* member).

ATA has been working on guidelines on this topic that should have substantial input from pediatric experts in US and Europe. This manuscript is not yet unpublished to our knowledge. It seems unlikely that an additional manuscript would be useful if we agree with the recommendations set out by the ATA group. Alan will check with Scott Rivkees for an update. The eventual plan would be to post the ATA paper on the website if all approve of its content. We look forward to any additional input from David who chaired this subcommittee.

9. ***“Safety of PTU in the Treatment of Pediatric Grave’s Disease”***: David Geller and Nicole Glaser. .

David Geller and Nicole Glaser prepared a summary of the issues surrounding this topic. This summary is posted in the “news alerts/drug shortages” section of the website.

Links to relevant articles on the topic (particularly Rivkees manuscript in IJPEM) will be added to the posting on the LWPES website.

10. **“GH neoplasia connection”**: Steve Waguespack (chair), JB Quintos, Adda Grimberg, Rona Sonabend (Ad-hoc member), ?Constantin?, ad-hoc members might include Lillian Meacham from Emory ([lmeacha@emory.edu](mailto:lmeacha@emory.edu)) and/or Charles Sklar at Sloan Kettering ([sklar@mskcc.org](mailto:sklar@mskcc.org))?

Steve agreed to chair this committee and is assembling his subcommittee and working on an outline for the manuscript. Steve continues to approach potential subcommittee members.

11. **Endocrine disruptors** – Catherine Gordon (chair), Sara Divall, Martin Draznin, Neils Skakkebaek (ad-hoc member), Ollie Soder (ad-hoc member): The BOD has asked the D+T to prepare a document on endocrine disruptors, similar to that prepared by the Endocrine Society, but from a pediatric perspective. It was suggested that this should be a comprehensive paper to include multiple clinical scenarios (precocious puberty, genital malformations, etc). Outside sub-committee members have been recruited, including toxicologists from Europe.

Our subcommittee has been assembled and we have developed an outline with assigned topics for each member. We are each beginning to work on our sections, in an effort to pull together a draft.

### Other issues:

**1. Drug safety alerts and shortages:** Sara Divall has been tracking potential drug shortages through the use of the American Society of Health System Pharmacists’ website ([www.ashp.org](http://www.ashp.org)). There is a section of the LWPES website in which these alerts are posted

Sara has been doing an outstanding job with this (thank you Sara!!!) and has developed the following surveillance strategy for drug safety alerts and shortages:

1. FDA Medwatch. <http://www.fda.gov/Safety/MedWatch/default.htm> Will send e-mail alerts for safety alerts on all drugs in addition to a monthly newsletter. Visits to the website are not necessary, as the email alerts keep me informed. There is another safety site from the health care notification network, which I find is not as good as the FDA site and pretty much recycles FDA alerts anyway.  
<https://www.hcnn.net/alerts/alerts.aspx>
2. For Drug Shortages: I first go to American Soc. Health system pharmacists site, as it is the most comprehensive and updated most often.  
<http://www.ashp.org/DrugShortages/Current/>. I try to look monthly for new shortages. Unfortunately, email alerts are not an option. FDA also has a site,  
<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm> but it is not as comprehensive or up to date.
3. The Endocrine Society emails a daily briefing to society members. Often times the daily briefings mention something about drug safety concerns or shortages even before the

FDA releases an alert or statement. The daily briefing compiles endocrine news from high impact medical journals and from news wires. Thus, can give me an idea of what drug information the public has heard and what they may ask their endocrinologist to clarify.

4. I am a regular reader of the New York Times which again gives me an idea of what the public is hearing.
2. The LWPES has proposed to work collaboratively with the NIH to establish permanent NICHD/FDA committee to monitor the safety and efficacy of pediatric medications in general, including reviews of pediatric endocrine medications. It is logical to propose that the D&T be represented on this board and take part in their regular meetings.

Scott Rivkees will likely be serving on this committee and Alan may be a member, as well. Additional members may be selected based on their specific areas of expertise in order to have representation of multiple fields of study. Alan will speak with Scott to report any new updates.

3. **Review on hGH book – Normal at Any Cost** (JB, David, Steve, Nicole, Adda, Catherine): A subcommittee was formed to evaluate this controversial new book. The subcommittee exchanged opinions via email and discussed this preliminarily with other LWPES committees. A draft of a statement intended to clarify current recommendations and approved GH uses for primary care pediatricians was written with the aim of publishing in the AAP newsletter.

The LWPES Ethics and Public Policy Committees weighed in on this issue, and we were advised not to comment publicly. There was a worry that our response would be viewed reactive rather than proactive.

4. **Survey on hGH brand switching (Adda, Catherine)**: Catherine and Adda have written up these data for publication and have submitted the manuscript – recently rejected by JCEM. They submitted the data to the PAS meeting and will be presenting in a poster session: Saturday, May 1, 2010, 1:00-4:00 pm.

Al made the suggestion to get feedback from Paul Thornton – Fort Worth, Karen Rubin – UConn, and Georgiana Klingensmith - regarding appropriate journals with a managed care focus. The *JCEM* review suggested that we target this type of journal rather than one read primarily by endocrinologists. Adda and Catherine plan to revise the manuscript based on feedback from JCEM and to resubmit.

#### **New initiatives:**

1. **E-blasts:** The D+T has made the decision that more frequent e-blasts would be helpful to the LWPES membership. While it has been agreed that we be very selective in what information is sent out to members and with what frequency, there is agreement that more frequent dissemination of clinical information

would be useful. Thanks to Steve Waguespack and Sara Divall for assistance in the drafting of e-blasts for BOD review.

- 2. Creation of Diabetes “suite” on the website** – with articles/guidelines pertaining to diabetes written by D&T or from other literature. We have not yet organized a separate suite, but did post a review of treatment recommendations for pediatric type 2 DM.

We should be on the lookout for relevant guidelines + clinical summaries – of educational value to pediatric endocrinologists – for this section of the website.

- 3. Meeting at PAS – Vancouver, Friday April 30<sup>th</sup>.** Per usual plan, we will ask representatives from the GH manufacturers to present data on adverse event rates. Thus far, Charmian Quigley from Lilly is confirmed to present data. Catherine and Nicole will work on inviting others. We expect the meeting to last 3 hours – 8:30-11:30.

- 4. Issues related to facilitation publication of manuscripts.** Approval process for manuscripts through BOD is fairly slow and cumbersome. Furthermore, many have encountered difficulty finding an appropriate “home” in a journal for manuscripts once completed, despite the official LWPES approval.

We spoke about suggested for facilitating these processes and discussion focuses on how to streamline submissions. As Alan suggested, we will generate a list of suggestions from the Committee for consideration by the BOD as to how to facilitate this process. We will also discuss this topic in more detail at our meeting in May.

***THANKS TO EVERYONE FOR THEIR HARD WORK!!***