

Accomplishments of the D&T 2008-09

D&T members:

- Outgoing members: Phil Zeitler, Daniele Pacaud (CPEG liaison), Anna Petryk, Madhu Misra
- Continuing Members 2009:
- Constantine Polychronakos (CPEG liaison)
- Nicole Glaser, Catherine Gordon (co-chairs, 2009-2010)
- Sara Divall, Andrea Haqq, Stuart Weinzimer, Adda Grimberg
- New Members 2009: Steve Gitelman, Steven Waguesnpac
- Chair Emeritus 2009: David Geller
- Ex-officio: Sally Radovick and Alan Rogol

In attendance at the Baltimore meeting:

David, Adda, Sara, Madhu, Daniele, Catherine, Anna

Subcommittee Papers:

1. *“Vitamin D deficiency in children and its management”* Madhu Misra (Chair), Daniele Pacaud, Mike Kappy, Paulo Solberg, Anna Petryk.

****PUBLISHED Pediatrics Aug;122(2):398-417.**

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

**** IN REVISION** to meet criteria for a State of the Art Review and to narrow the focus are being incorporated. The Final draft anticipated this summer, followed by resubmission to BOD in summer 09.

3. *“Aspects of pediatric thyroid treatment”* (effect of soy, pharmacy directives for taking l-T₄ on an empty stomach): Phil Zeitler & Paulo Collett-Solberg.

**** SUBMITTED “letter” to the LWPES BOD (? and the Chair of the AAP Section on Endocrinology).** Awaiting decision on merit. Assuming both "Boards" agree, to be submitted in Letter format to Pediatrics.

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

**** D&T COMPLETED ITS PRE-REVIEW.** Arlan and Daniele provided final edits and recommendations. Phil provided table of recommendations. Per Alan’s instructions, this Guidelines paper will be sent by Alan to the BOD, who will assign a

corresponding editor and will outsource to 2 ad hoc reviewers. Plan is to submit to journals targeting both ICU/ER physicians (for earlier recognition and appropriate therapy), and general pediatrics readers (e.g., Pediatrics).

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

**** SUBMITTED TO BOD- AWAITING APPROVAL. 2 ad hoc reviewers this manuscript, one of whose comments Alan has disseminated to the manuscript authors. We hope to receive the 2nd reviewer’s comments within the week. It is anticipated that there will not be any substantive changes required, and the manuscript will be approved for submission to Pediatrics without further delay or need for additional BOD review.**

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

**** IN PREPARATION- SUMMER SUBMISSION TO D&T/BOD. Nicole and Anna have expanded several sections from the initial draft. Steve Gitelman, David Geller (and later, Mary Malloy [Cardiology, UCSF]) will complete the first draft of this manuscript within the next few weeks, for review by BOD. This manuscript is intended as a review/emerging concepts/state of the art manuscript, rather than a treatment guidelines paper, as too little RCT data are available at this time.**

New Subcommittees Formed:

1. ***“Bariatric surgery in children”***: ***Andrea Haqq will serve as chair of this subcommittee.*** Leona Cutler has expressed interest in serving as an *Ad hoc* member and the remainder of the subcommittee is being formed. Dr. Helmtrath of Bariatric Surgery at UNC has agreed to represent the surgery side.

**** ASSEMBLING ROSTER OF AUTHORS- In addition to Dr. Helmtrath, Andrea has asked Leona Cutler and both Steve Gitelman and Steve Waguespac to consider involvement in this project.**

2. Replacement manuscript ***“Guidelines for the use of growth hormone in children”*** (*Journal of Pediatrics* 2003; 143(4): 415-421.) As requested by the BOD, the older manuscripts listed on the LWPES website were reviewed for possible update and/or retirement. This manuscript 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.*

*** Adda Grimberg will chair this sub-committee; Sara Divall and Constantine Polychronakis (CPEG rep to the D&T) will also represent the D&T. Requests for participation were made to 2-3 other individuals, serving as ad hoc members. 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. ↓*

*** NOTE: Barbra Lippe referenced a JAMA article from 4-1-09 recommending that authors of Guidelines papers to be endorsed by or emanating from Professional Medical Associations must have zero financial relationship with manufacturers of the products endorsed...may be difficult to find authors without ties to GH companies.*

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

*** TO BE REVISITED? The need for a separate D&T paper to consider the use of RAI (vs. medical therapy/surgery) in the treatment of pediatric GD remains unclear. The ATA completed their review in December 2008 which contains sections devoted to pediatric GD. This document is under review by ESPE and LWPES thyroidologists. The BOD may consider asking a D&T member, in conjunction with an ad hoc reviewer from among the membership to review the ATA guideline. Pending their recommendations, we will reconsider the need for a separate LWPES document.*

A related issue surfaced in the past year: concern as to the safety of PTU in the treatment of Pediatric GD. The NICHD hosted a workshop in October 08, attended by several LWPES members (Scott Rivkees, Roz Brown, Surendra Varma [AAP liaison]). The NICHD noted the need for further study of this issue. After subsequent conference call (David Geller, Charley Stanley, Nicole Glaser, Surendra Varma, Don Mattison of the NICHD), *letters were drafted to both NICHD and FDA requesting they convene formal pediatric committees to annotate adverse event frequency in pediatrics*, and to determine whether changes in PTU prescribing information are needed. *A summary paragraph of the bullet points taken from the workshop notes was crafted by Nicole and David and presented to the BOD for pre-review, with the intention of posting on the website and disseminating via blast e-mail to the membership.* NEJM recently published a letter to its editors authored by Rivkees/Mattison requesting that PTU be discontinued as first line therapy in childhood GD. *Addendum: based on this, the Endo Society “scooped” us by issuing a call for PTU use to be discontinued in pediatrics*

(Stephanie Kutler, blast e-mail, 4-14). Alan will update the status of the BOD decision to alert our members via blast e-mail.

**** NOTE: It is unclear whether the BOD approved these letters, and if so, whether they were sent to either the FDA or the NICHD. Addressing Dorothy Becker's question, I have not been able to verify that our 1-page summary of the workshop findings was ever posted on our website or sent via blast e-mail to the membership.**

Other issues:

1. Solicit membership suggestions for new manuscripts/topics for research- Phil Zeitler recently recommended consideration of a Peds Endo Guidelines for the management of hyperglycemia and diabetes in the ICU and/or post-op diabetic child, given the increased attention paid to this in the adult endocrine literature.

To be reconsidered by the D&T later this year, pending a pre-review of the existing literature to determine the need for this at the present time.

2. Tracking potential drug shortages through the use of the American Society of Health System Pharmacists' website (www.ashp.org). The D&T would designate one of its members to review the Drug Shortages section of the website monthly, in order to bring to the attention of our membership shortages specific to endocrine medications.

Sara Divall volunteered to monitor this website and to provide the D&T recommendations for the purpose of notifying our membership (via the website) as well as to contact manufacturers of these products as shortages arise. We also recommended to the BOD that there be a link on the website which could archive all medications that are unavailable, and would provide updates on the status of new production as well as alternative therapies.

3. 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.

Awaiting the BOD directive before soliciting D&T volunteers to sit on these committees.

4. As requested by the BOD, all papers on the website 3 years and older were reviewed by a D&T committee member to determine whether to retain, retire or revise the manuscript. The 2003 guidelines on the use of GH manuscript will be revised (see above), and the 1995 guidelines retired. The 2002 CAH consensus statement remains current (Miller), as does the 2004 discussion of the management of menstruation in the developmentally delayed female (Divall,

Rossi), and the 2004 consensus statement on DKA management (Glaser). The 2005 paper discussing the treatment of Pediatric bone disease is to be replaced by the Ward, *et al* Bisphosphonates paper.

The committee agreed that the 2002 document on the GH-neoplasia connection requires updating, particularly in light of the information derived from database mining of the Lilly and Genentech registries regarding second neoplasms in GH-treated patients, both those who received Rad Tx and those who didn't. The D&T will consider authors for this revision.

The D&T committee members expressed concern that the timeline for completing and submitting manuscripts of a review/state of the art type is too protracted. In our meeting it was suggested that there be imposed a 1-year time limit on completing these manuscripts, from time of manuscript development to final review, and a 2-3 month “window” for the BOD to return manuscripts sent to them for review. I brought this up to little response at the BOD meeting, with only Dr. Rosenfield commenting.

Regarding the BOD review process, the D&T recommended that Review manuscripts be read by 2 members of the BOD (rather than a single reviewer), and that these reviewers engage in preliminary discourse to derive a BOD “consensus”- the concern being that by the time the BOD receives these manuscripts, the paper has already been endorsed following several iterations, only to be rejected by a single reviewer. Dr. Rosenfield noted that even State of the Art/Review manuscripts are reviewed by one BOD and one outside reviewer.

Appendix 2

LWPES D&T Manuscript Submission and Authorship Policies

A. Procedure for manuscript submission:

Nature of manuscript:

1. Position papers/Policy statements: will go through an extensive review process

Distributed within Subcommittee→Revised and circulated within D&T Committee→Revised manuscript → Alan Rogol/Sally Radovick→ preliminary comments → Revised manuscript → Alan Rogol/Sally Radovick → Board of Directors→ One internal and two external (or two external and one internal) Reviewers → detailed comments → Revised manuscript → Alan Rogol/Sally Radovick → Membership at large (posted at website for a month)→ more comments → screened by Alan Rogol/Sally Radovick → Revised manuscript → D&T subcommittee and D&T→Revised manuscript→ Alan Rogol/Sally Radovick → back to authors to submit to a journal of choice

2. Consensus Statement: Process will be more streamlined, and the statement will go to the BOD, but will not be sent out to the membership at large to review

3. State of the art reviews: Will also involve a more streamlined process for the review. The statement will go to the BOD, but will not be sent out to the membership at large to review

B. Letter to accompany article during its submission to the journal detailing (as much or as little) the review process and stating clearly what kind of manuscript this is:

‘We are submitting a manuscript titled “-----” for consideration for publication in --- as a State of the Art Report. This submission is on behalf of the Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. In this review, we discuss ---.

This report has been extensively reviewed by experts in the field prior to submission to -- -, as part of the process for submission of such reports based on LWPES guidelines. The report was first reviewed by a panel of three expert reviewers (one internal and two external) selected by the Board of Directors of the LWPES, and after the comments and suggestions of these reviewers were addressed, the report was made available to all LWPES members to review. Further modifications were based on comments and suggestions of LWPES members at large.’

For Reviews: To be included in the title page: "This review was developed to be of educational value to practitioners. It should not be construed as indicating official policy or guidelines of the Lawson Wilkins Pediatric Endocrine Society".

For Position Statements/Policy Statements: The BOD will come up with a stronger statement of support from the LWPES.

C. Manuscript authorship:

A. Authorship will be confined to individuals who made substantive contributions to a manuscript. Ordinarily, this will constitute only the members of each subcommittee. However, additional authors may be included at the discretion of the subcommittee chair in cases where a significant contribution to the project has taken place.

B. All D & T members who reviewed a manuscript will be listed by name in the acknowledgment section of the manuscript: ‘We thank the following current and past members of the Lawson Wilkins Pediatric Endocrine Society (LWPES) Drug and Therapeutics Committee for careful review of the manuscript and constructive comments: -----’. We also thank the three expert reviewers selected by the Board of Directors of the LWPES to review and critique this manuscript.’

Appendix 3
Annual Timeline for the Drug and Therapeutics Committee of the LWPES

1. Members of the D & T Committee will meet in conjunction with the LWPES meeting each spring. The agenda will include the following:
 - Welcome and introduction of new members
 - Progress report by subcommittee chairs regarding the status of various projects
 - Safety updates to be given by representatives from major pharmaceutical companies that manufacture growth hormone or other products widely prescribed by pediatric endocrinologists
 - Identification of new projects with formation of committees and appointment of committee chairs (volunteers may be solicited to join specific committees after the meeting as well)
 - Suggestions of LWPES members to be nominated for membership in the D & T committee (to be communicated to the executive board and President of the society)
 - Other business

A summary presentation of D & T committee activities will then be made by the Chair to the LWPES executive board and to the LWPES membership at large during the annual business meeting.

After the conference, meetings of the D & T committee meeting will be circulated by the Chair to the committee membership.

2. Telephone conference #1 to be held in August. The priority will be to include subcommittee chairs with as many members participating as possible. Subcommittee chairs will provide updates and timelines on various projects, for example; anticipated outline and subsequent manuscript completion date for review papers and position statements, status of submitted, revised or rejected manuscripts, progress made in organizing consensus conferences, updates on drug shortages, etc.
3. Telephone conference #2 to be held in February. Any reports that have been circulated since the previous teleconference will be discussed. Again, updates will be provided by the various subcommittee chairs on their various projects. Tentative information will be provided regarding the projected date and time of the D & T committee meeting in May. It is anticipated that subcommittee projects will progress from inception to completion of a finished product within a maximum of one year.