Chair’s Update
Jeffrey Hord, MD, FAAP

The success of the AAP Section on Hematology Oncology (SOHO) depends upon the volunteer efforts of its members and collaboration with other groups working toward similar goals. I am so grateful for the numerous Section members who have stepped forward in 2014 to do the work of the Section. Seven clinically based review groups were established in early 2014 as part of the collaboration between SOHO and the American Society of Pediatric Hematology/Oncology (ASPHO). We received over 60 responses to the request for volunteers and 42 PHO physicians who were members of both organizations were divided into the various groups based upon areas of expertise. Thus far, these groups have provided input on 9 PHO related payer policies, 11 book chapters, 3 draft AAP policy statements and 1 external policy. Other Section members have volunteered to be part of 2 new Section subcommittees - the Communication Subcommittee chaired by Dr. Carl Allen and the Education Subcommittee chaired by Dr. Eric Werner. The Communication Subcommittee will be responsible for producing the Section newsletters and the content of the Section website. The Education Subcommittee will be coordinating the Section’s efforts to educate general pediatricians and patients/families about pediatric hematology/oncology (PHO) topics. One of the first things this subcommittee accomplished was to submit 4 PHO topics for consideration to be presented at the 2015 AAP National Conference and Exhibition and all 4 were accepted.

Believing that there is strength in numbers, SOHO continues to work with other advocacy, professional, and accreditation organizations. Two Section members were appointed earlier this year as liaisons to such organizations - Dr. David Dickens to the Alliance for Childhood Cancer and Dr. Maria Velez to the American College of Surgeons Commission on Cancer. We welcome Dr. Rebecka Meyers from the Section on Surgery as a liaison to our Section. To engage younger members and to gain their perspective, we are proposing a bylaw change which would allow a PHO fellow in training to be part of the SOHO Executive Committee. This bylaw change will be part of the election ballot that you will receive in March, 2015.

Throughout the past couple of years, the leadership of SOHO and ASPHO developed an alliance to collaborate especially in the areas of advocacy and policy review. The accomplishments of the alliance were significant and included the development of the previously mentioned policy review groups, a joint advocacy agenda and PHO advocacy education sessions held at the last two Annual ASPHO Meetings. One setback has been the failure to sustain the gain in AAP membership needed to fund the

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Chair's Update

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alliance. Alternative alliance models are being explored which extend beyond our subspecialty. In March 2015, the AAP is holding a Summit with representatives from the various pediatric subspecialty sections. The goal of this meeting is to brainstorm about the Academy's subspecialty strategy, including the best ways to connect Sections with subspecialty professional societies.

A revision of the policy statement “Standards for Pediatric Cancer Centers” (formerly “Guidelines for Pediatric Cancer Centers) was published in the August, 2014 issue of Pediatrics (http://pediatrics.aappublications.org/content/134/2/410.full.pdf+html). There are several statements in various stages of revision: Cord Blood Banking for Potential Future Transplantation, Preservation of Fertility in Pediatric and Adolescent Patients with Cancer and Children as Hematopoietic Stem Cell Donors.

I strongly encourage each of you to consider how you might share your expertise and talent to build a stronger SOHO. I think you will find that your professional development and your interactions with colleagues will be enhanced through active participation in the work of the Section.

Welcome to Our New Members

If you know of others who might be interested in joining the Academy and the Section please refer them to: www.aap.org/en-us/pages/become-member.aspx

The Section on Hematology/Oncology welcomes the following members: http://www2.aap.org/attachments/SOHO_Welcome_to_New_Member_List.docx

For Upcoming Newsletters . . .

We welcome your input and encourage you to submit ideas or information by email to Carl Allen, MD FAAP at callen@txch.org or Suzanne Kirkwood at skirkwood@aap.org for future issues of the newsletter.

Statements and opinions expressed in this publication are those of the authors and not necessarily those of the American Academy of Pediatrics or the AAP Section on Hematology/Oncology.
The newly-formed Communications Subcommittee is charged with oversight and publication of SOHO newsletters and maintaining the Section website. The Subcommittee, [http://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/section-hematology-oncology/Pages/Subcommittees.aspx](http://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/section-hematology-oncology/Pages/Subcommittees.aspx) appreciates the opportunity to share this newly enhanced edition of the semi-annual with SOHO membership. The purpose of the newsletter is to provide a forum for discussion of Section activities within the AAP as well as relevant issues within the field of Pediatric Hematology-Oncology. New features in this newsletter include highlights of significant research publications by Dr. Mary Jane Hogan and Dr. Taizo Nakano; “Tech Tip” highlighting potentially interesting new tools and technology; a guest column from the Section on Hospice & Palliative Medicine by Dr. Justin Baker; updates on AAP activities of special interest for SOHO by Dr. David Dickens (Alliance for Childhood Cancer and Advocacy Initiatives Liaison), Dr. Maria Velez (ACoS Commission on Cancer Liaison), Dr. Gary Crouch (Council on Pediatric Subspecialties Representative), and Dr. Rebecka Meyers (Section on Surgery Liaison). Finally, Dr. Lewis Hsu and Dr. Aniket Saha summarize the 2014 NHLBI Guidelines regarding the Management of Sickle Cell Disease as a Featured Topic. The website will continue to be a resource for Section members, and we will work over the next months to optimize resources for and communication with our colleagues in General Pediatrics as well as other AAP Sections. Please contact us with any feedback on the SOHO newsletter or website. We also welcome any ideas for contributions to the newsletter or website.

A primary mission of the SOHO is to improve the care of children with hematologic and oncologic disorders through education. The SOHO Education Subcommittee [http://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/section-hematology-oncology/Pages/Subcommittees.aspx](http://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/section-hematology-oncology/Pages/Subcommittees.aspx) was established to assist the Executive Committee in:

- The development of educational programming regarding hematology/oncology conditions for general pediatricians;
- Identifying pediatric hematology/oncology topics of broad interest for the AAP News Focus on Subspecialties column;
- The review of existing information and development of new content regarding pediatric hematology/oncology conditions for parents and consumers.

The SOHO is the voice of pediatric hematologists/oncologists within the AAP. One of the ways that this is achieved is by developing and submitting PHO related topic proposals for the AAP National Conference and Exhibition (NCE) that is held each fall. This year the NCE was held on October 11-14, 2014 in San Diego, California.

The PHO sessions that were offered for the 2014 and will be offered for 2015 are:

**2014**

1. Anemia in Children: Iron Deficiency and Beyond – George Buchanan, MD, FAAP
2. Bleeding Disorders in Adolescents with Dysfunctional Uterine Bleeding: Whom to study and what to order? – Guy Young, MD, FAAP
3. Early Recognition of Childhood Cancer Syndromes – Zora Rogers, MD, FAAP
4. The Current Epidemic of Thrombosis in Children and Adolescents: How to Recognize, Prevent and Treat - Guy Young, MD, FAAP

Dr. Buchanan also represented the Section and pediatric hematology/oncology at an “Exploring Pediatric Subspecialties” session for medical students sponsored by the Section on Medical Students, Residents and Training Fellows.

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2015
2. Iron: Too Little or Too Much? - Brigitta Mueller, MD, FAAP
3. Clots and Kids: An Increasing Problem – Shannon Carpenter, MD, FAAP

In addition, the Section has the opportunity to provide content for the AAP News Focus on Subspecialties column on an annual basis. This content focuses on pediatric hematology/oncology topics that are of broad interest to general pediatricians and other subspecialists. Thank you to Dr. Denise Adams for collaborating with the Dr. Marilyn Liang of the Section on Dermatology in writing the article, “Treatment of vascular anomalies advancing, but more research needed” (http://aapnews.aappublications.org/content/35/10/12.full.pdf+html) for the October edition. A listing of the other articles that have been contributed by SOHO can be found on the website at: http://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/section-hematology-oncology/Pages/Newsletters-and-Publications.aspx

Finally, www.HealthyChildren.org is the Academy’s website for parents and caregivers. One of the goals of the subcommittee is to review and revise current PHO content and explore the development of new articles. We plan to engage in this process in 2015.

Hot Papers in Pediatric Hematology/Oncology

Reviewed by: Mary Jane Hogan, MD, FAAP, Assistant Clinical Professor, Pediatric Hematology Oncology, Yale University School of Medicine, New Haven, Connecticut.


Between April 2012 and February 2014, 25 children with relapsed or refractory acute lymphoblastic leukemia from Children's Hospital of Philadelphia, and 5 adults with similar disease from University of Pennsylvania School of Medicine were infused with autologous chimeric antigen receptor-modified T cells targeting CD 19 (CTL019). The study found that 27 of 30 patients (90%) experienced complete remissions, including 15 treated with prior hematopoietic stem cell transplant (SCT) and 2 treated with prior blinatumomab, a CD19-directed bispecific antibody. Of the 27 patients who achieved a complete remission, 5 withdrew from the study for alternate therapy, three of whom were treated with allogeneic SCT and in remission 7 to 12 months after CTL019 infusion.

Fifteen patients achieved a sustained remission with no further therapy at a median follow-up of seven months. The probability of 6-month event-free survival was 67% (95% CI, 51% to 88%) and overall survival was 78% (95% CI, 65% to 95%). Probability of six-month CTL019 persistence was 68% (95% CI, 50 to 92%) and relapse-free B cell aplasia was 73% (95% CI, 57 to 97%). Sustained remissions for up to 2 years, observed in these 15 patients, were associated with quantitative PCR-detectable CTL019 sequences and B cell aplasia.

All patients experienced cytokine release syndrome. Eight patients (27%) developed severe symptoms which were associated with higher disease burden and effectively treated with tocilizumab, an IL-6 receptor antibody. Thirteen patients (43%) had neurologic toxicities, ranging from febrile delirium to global encephalopathy, which completely resolved without additional intervention or apparent chronic implications.


Investigators from multiple, international research centers, led by St. Jude Children's Research Hospital, obtained microarray gene-expression profiling of 1725 individuals, ages 1 to 39, diagnosed with precursor B-cell acute lymphoblastic
leukemias (ALL) to determine the frequency, diversity and tyrosine kinase inhibitor responsiveness of genetic alterations in Philadelphia chromosome-like ALL (Ph-like ALL). Individuals with Ph-like ALL do not possess the BCR-ABL1 fusion protein from the t(9;22)(q34;q11.2) Philadelphia chromosome, but have a similar gene-expression profile, alterations of the lymphoid transcription factor gene, IKZF1, and poor outcomes as patients with BCR-ABL1 positive ALL. Next-generation sequencing to identify genetic alterations that cause Ph-like ALL was performed on 154 patients. Mouse pre-B cells and xenografts of human Ph-like ALL were examined for functional effects of fusion proteins and tyrosine kinase inhibitor efficacy.

The frequency of Ph-like ALL increased with age and was associated with poor survival compared to other precursor B-cell ALL. Overall, 264 (15.3%) patients possessed Ph-like ALL, ranging from 10% of children, ages 1 to 9, with standard risk ALL, to 27% of adults, ages 21 to 39, with ALL. Among patients with Ph-like ALL, 5 year overall survival rate for children, adolescents and young adults was 62%, compared to 91% for the same ages without Ph-like ALL.

Alterations involving kinase signalling or cytokine receptor activation were discovered in 91% of patients with Ph-like ALL including rearrangements in ABL1, ABL2, CRLF2, CSF1R, EPOR, JAK2, NTRK3, PDGFRB, PTK2B, TSLP, or TYK2 and sequence mutations in FLT3, IL7R, or SH2B3.New subgroups of Ph-like ALL sensitive in vitro to dasatinib included ABL1, ABL2, CSF1R, and PDGFRB fusions, ruxolitinib-sensitivity included EPOR and JAK2 rearrangements and crizotinib-sensitivity was associated with ETV6–NTRK3 fusion. Additional investigations in older adult Ph-like subtypes and clinical trials identifying Ph-like ALL are needed to assess the efficacy of adding tyrosine kinase inhibitors to current therapy regimens.


An open-label, randomized phase III study by investigators from Blood and Marrow Transplant Clinical Trials Network was conducted to compare outcomes between children with hematologic cancer undergoing double unit (n=111) or single-unit cord blood transplantation (n=113) after a uniform myeloablative conditioning regimen and graft-versus-host disease (GVHD) prophylaxis. Between December 2006 and February 2013, children, ages 1 to 21 years, diagnosed with acute myelogenous leukemia, acute lymphocytic leukemia, acute biphenotypic leukemia, myelodysplastic syndrome or chronic myeloid leukemia received cord blood HLA matched to at least 4 of 6 different loci, with the first unit at least 2.5 x 10⁷ nucleated cells /kg of body weight, and the second unit, at least 1.5 x 10⁷ nucleated cells/ kg of body weight. All patients received a conditioning regimen of fludarabine, total body irradiation, and cyclophosphamide, and post transplant GVHD prophylaxis of cyclosporine for 6 months with subsequent tapering, and mycophenolate mofetil for 45 days (or longer depending upon GVHD status).

Both groups were matched for sex, age, cytomegalovirus status, disease type, self-reported race, degree of donor-recipient HLA matching, and status at transplantation. Overall survival at 1 year was 65% (95% CI, 56 to 74) for double-unit recipients and 73% (95% CI, 63 to 80) for single-unit recipients. Hazard ratio for mortality was 1.34 (95% CI: 0.86 - 2.09; P = .20) for double-unit vs single-unit recipients. There were no differences in rates of disease-free survival, neutrophil and immunologic recovery, transplantation-related mortality, relapse, infections, acute and chronic GVHD. However, single unit recipients had higher (76% vs 65%; P = .04) and sooner platelet recovery (58 days vs 84 days) than those who received double units. In addition, one unit recipients had lower rates of grade III and IV acute and chronic GVHD (13% vs 23%; P = .02) than two unit recipients. The authors conclude that given the difficulty finding in HLA compatible donors, double unit cord blood transplantation did not confer significant additional benefit over single unit.

Reviewed by: Taizo Nakano, MD, FAAP, Assistant Professor, Pediatrics, Center for Cancer and Blood Disorders Children's Hospital Colorado, University of Colorado School of Medicine


In hemophilia B, a small increase in the factor IX percentage can move a patient from the severe to moderate deficiency category, thereby greatly reducing both the incidence of severe bleeds and use of factor product. This same principle
behind prophylactic factor replacement that is now standard care for severe hemophilia patients also drives the pursuit of gene therapy. The goal is to finally replace the chronic administration of recombinant factor products with a single infusion resulting in long-term expression of factor IX. The study carried out by Nathwani et al. represents the efforts of an international collaboration of hematologists to move gene therapy from the bench to the bedside and provide a less invasive, less expensive, and importantly, a curative approach to hemophilia B.

Their use of a novel self-complimentary adeno-associated serotype virus (AAV8) led to successful in vivo expression of factor IX in a pilot study previously published (N Engl J Med 2011;365:2357-2365). Building on that success, the current study evaluates the stability of transgene expression and the long-term safety in 10 patients with severe hemophilia B. The manuscript reports long-term, albeit low level, therapeutic factor IX expression and clinical improvement in all 10 patients infused with a single dose of AAV8 vector. Furthermore, no late toxic effects were reported after 3 years of follow up. Their success represents an important milestone in the pursuit of gene therapy that could translate into applications for numerous blood protein deficiencies.


The past decade produced a number of monumental trials that reshaped the care of pediatric patients with sickle cell anemia. With a focus on preventative care, the results of these trials were recently summarized in an evidence-based publication, Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members (JAMA 2014;312(10):1033-48). Beginning the next chapter to reshape sickle cell care, Debaun et al. aimed to study a persistent concern in the sickle cell community, the silent cerebral infarct. Though it is known to increase risk for symptomatic stroke, poor academic achievement, and lower IQ, we lack standardized guidelines to diagnose, monitor and treat this common neurologic injury.

The Silent Cerebral Infarct Multi-Center Clinical Trial (SIT) set out to determine whether blood-transfusion therapy can prevent an end-point of stroke or new or enlarged silent cerebral infarct. The authors carried out a multicenter, randomized trial that assigned 196 children with sickle cell anemia-related silent cerebral infarcts to either receive standard observational care or blood-transfusion therapy. After a median follow up of 3 years, 6% of children in the transfusion group experienced an end-point complication compared to 14% of children in the observation group. They conclude that blood-transfusion therapy significantly reduces the incidence of recurrent cerebral infarct in children with sickle cell anemia and propose a potential opportunity to impact the long-term burden of neurologic injury in this patient population.


Recognizing the rapid progress in recent years to understand primary thrombotic microangiopathy (TMA), the authors present a thorough review to better define and classify TMA syndromes. They summarize our current understanding of the pathogenesis, management, and outcomes of these syndromes and move away from ambiguous terms like “atypical” and “idiopathic”. Nine primary disorders are presented taking note of important historical milestones that help to identify both their common clinical features and unique differences. A focus on both acquired and hereditary complement-mediated TMA provides a platform for continued discussion on the role of anticompliment therapy. Overall, the review highlights how the field’s great successes have reduced mortality and revealed previously unrecognized long-term morbidities.
PHO Tech Tip

In this feature we hope to highlight various technologies that have been developed to assist pediatric hematology/oncology patients with their care and pediatric hematology/oncology physicians in caring for their patients.* If you have a tech tip that you would like to be shared in future editions of the newsletter, please send them to: Suzanne Kirkwood at skirkwood@aap.org

VOICE Crisis Alert (http://crisisvoice.com/)

This free app was developed for patients with sickle cell disease to record a pain event, communicate it to a contact(s) of choice, view pain history, and view/edit a Crisis Care summary page. It has been tested to run on most devices running Apple IOS (iPhone, iPad, iPod Touch, etc.) or Android operating systems. Windows Mobile, however, is currently not supported.

Pain Squad Mobile App

The Hospital for Sick Children in Toronto (or SickKids) needed to find a way to encourage their young cancer patients to complete daily reports on their pain. With a little back-up from Canada's top police dramas, an innovative mobile app made this overwhelming task easy and fun. This app is free to download from the Apple Store. Read about the development of the app (http://www.sickkids.ca/AboutSickKids/Newsroom/Past-News/2012/iphone-app-helps-with-cancer-pain.html) and view a video regarding the app (http://www.campaignpage.ca/sickkidsapp/)

*Inclusion of this information within the newsletter does not represent endorsement of the product by the AAP or the Section on Hematology/Oncology, but is being shared as an information only.

Featured AAP Section: Section on Hospice and Palliative Medicine

Integrating Palliative Care into the Ongoing Care of Children with Cancer
It Takes a Village and It Starts with the Primary Oncology Team

Justin N. Baker, MD, FAAP, FAAHPM
Chief, Division of Quality of Life and Palliative Care
Attending Physician, Quality of Life Service
Director, Hematology/Oncology Fellowship Program
Associate Member, Department of Oncology
St Jude Children's Research Hospital
Member, AAP Section on Hospice and Palliative Medicine

More than 12,000 children in the US will be diagnosed with cancer in 2015. Of these children, 2000 will die from their cancer or treatment-related issues. Two thousand is 2000 too many and we must continue to fight to find cures and save children because, as Danny Thomas once said, and we all believe, “No Child Should Die in the Dawn of Life.” Beyond these statistics, however, lies the terrible truth of why I wanted to write this piece – SUFFERING, and what to do about it. Suffering is a terrible word and a far worse condition. The amount of suffering that a patient and family must endure while pursuing cure is simply overwhelming, and too many times that pursuit still ends in increasing suffering and death. Suffering comes in many forms: pain and symptoms (some related to the treatments we inflict on these kiddos and their families in our pursuit of cure), social morbidity due to family disruption, psychological strain from having to contemplate issues of life and death at far too young an age (both the child/patient and their caregivers),
financial devastation, spiritual isolation/existential distress and, trying to maintain hope in the midst of tremendous uncertainty and innumerable other sources of suffering.

In a recent review by Waldman and Wolfe (PMID: 23337915), we were told that in treating children with cancer and their families, “palliative care is simply a novel term for the total care of a child and family, an approach that should be applied consistently and concurrently regardless of disease status.” I could not agree more! Integration of palliative care into the ongoing care of children with cancer must therefore be an urgent, upstream priority and it must start with the primary cancer team.

Integrating key pediatric palliative care (PPC) concepts can help address suffering and incorporate an emphasis on quality of life into the overall care plan from the point of diagnosis of cancer. Many oncology teams do this very well, but, it is a somewhat “silo”ed approach where the “medical team” deals with disease- and physical symptom-related issues while the “psycho-social team” deals with, well, everything else. Pediatric palliative care must be conceptualized as always being a part of the care paradigm, allowing for the transition to predominantly comfort care to occur gradually and intuitively, but also allowing for the integration of palliative care resources and expertise into the care plan at an earlier stage (preferably at the very beginning) of the illness trajectory. Indeed, by viewing palliative care as primarily oriented toward the quality of life experienced by the child and family from the start of the child’s illness, if there comes a point at which potentially curative therapy is no longer available, the continuation of attention to quality of life will not be a line ‘drawn in the sand’ between ‘curative care’ and ‘palliative care’ but will rather be a continued attention to the way the child experiences his or her day. Such a philosophy of care says to a child, ‘The first day you come to clinic with an illness we care about the quality of your life. If ever the disease progresses or relapses, we care about the quality of your life. And if the day comes when we have no more curative therapies for you, still we care about the quality of your life. This includes the last days of your life – always, we care about the quality of your life.’ Such an approach takes away the false sense that ‘palliative care’ is something new in a child’s experience. It is not.

Figure 1 demonstrates that resources, education and policies need to be developed and implemented at the institutional level – for ALL children and their families. Practically speaking, at our institution this has led to the development of a policy requiring all clinical nursing staff to be trained and certified in a 2-day End-of-Life Nursing Education Consortium (ELNEC) course that our PPC team provides as well as another 8 CEU PPC course that we have developed. Many people have termed this a generalist approach toward PPC integration. Resources are obviously required in order to develop and implement these policies and educational endeavors. A robust, “face of PPC” consult team, must also be developed. This team must have exquisite consultant etiquette and a “yes”/”git er dun” approach toward partnering with the primary oncology team. A GREAT place to start is in simply asking the oncology team how the PPC team may best be of service to their patients and families as well as how they can help the primary team do their job more efficiently and effectively. The final point on integration that you may consider would be a “trigger-based” approach to integration of all or parts of the PPC team for specific “high-risk” populations. Ocenga and Friebert (through the Center to Advance Palliative Care – CAPC) have created a very helpful list of diseases to consider when creating a trigger-based intervention. You may choose to use this list or you may decide to develop a “trigger-based” approach that is more specifically tailored to meet the needs of your institution. Other ideas we have utilized include a home-based approach to palliative care assessment and intervention that is only accessible through our PPC team as well as an ICU-based point of trigger-based integration that is based on length of stay in the ICU rather than being risk or disease specific.

Figure 1.
In sum, integrating palliative care into the ongoing care of children with cancer takes a village, but it must start with the strong primary home – the oncology team. It is the careful, evidence-based, attentive response to supporting those things that make a child's life good, a child's days good, and a family's experience meaningful. Articulated in this way, palliative care is something that should be welcome from the start, not a marker for the end of life. Such an approach allows clinicians to be present at all points of a child's illness trajectory, including, in a non-threatening way, at the end of a child's life. In order to optimize these points of integration, those of us in the PPC field must come alongside our oncology colleagues as we work hand-in-hand to address the horrific suffering of these children and their families.

Figure 2. A Model of Integrating PPC concepts into Pediatric Oncology*

*Modified from: Levine D¹, Lam CG², Cunningham MJ³, Remke S⁴, Chrastek J⁵, Klick J⁶, Macauley R⁷, Baker JN¹. Best practices for pediatric palliative cancer care: a primer for clinical providers. J Support Oncol. 2013 Sep;11(3):114-25

Consider Consultation with Pediatric Palliative Care Team

*Modified from: Levine D¹, Lam CG², Cunningham MJ³, Remke S⁴, Chrastek J⁵, Klick J⁶, Macauley R⁷, Baker JN¹. Best practices for pediatric palliative cancer care: a primer for clinical providers. J Support Oncol. 2013 Sep;11(3):114-25
The Alliance for Childhood Cancer (ACC) (http://www.allianceforchildhoodcancer.org/) was established in September, 2001 to bring together patient advocacy groups within the medical and scientific community. This collaborative work is intended to advance the needs of pediatric oncology patients in the areas of education, diagnosis, treatment and research. A listing of the member organizations can be found at: http://www.allianceforchildhoodcancer.org/memberorgs

The American Academy of Pediatrics has been a member organization of this group since its inception with representation through a pediatric hematology/oncology liaison and the AAP Department of Federal Affairs staff. Dr. Edwin Forman, MD FAAP, a founding member of the ACC, has served as the liaison on behalf of the Academy and the Section on Hematology/Oncology (SOHO) for the past 10 years. I have assumed this role as of, August 1, 2014 and had the opportunity to participate in several meetings in Washington, D.C. on behalf of the Academy during September and October, 2014.

The annual Congressional Childhood Cancer Summit was held on September 19, 2014 at the U. S. Capitol Visitor Center and was led by Dr. Frances Collins, Director of the National Institutes of Health (NIH). Later that day, a White House briefing on pediatric cancer was held at the White House Executive Office Building and was led by the Office of Public Engagement with Dr. Harold Varmus, Director of the NCI as the keynote speaker. Finally, a policy roundtable was held by the ACC on September 20, 2014.

Below is a summary of the discussion items raised throughout the two day event:

**Increasing Funding for Pediatric Cancer Research**

The White House Chief Officer of Management and Budget indicated difficulties in recommending additional allocations toward the NIH and suggested the Department of Defense (DOD) as a potential additional funding stream. The Director of Congressionally Directed Medical Research for the DOD (COL Wanda Salzer) was supportive of this concept. Dr. Collins cited a decrease in overall NIH funding, encouraged support from the ACC and recommended discussion with the National Cancer Institute (NCI) to enhance the fundability of pediatric-focused research. Dr. Varmus (NCI) indicated that funds are allocated according to the quality and innovation of the proposals rather than in a disease or age specific way.

**Promoting Legislation that Enhances Pediatric Research**

- Possible revision of existing laws including the Best Pharmaceuticals for Children Act and Pediatric Research Equity Act.
- The Carolyn Price Walker (CPW) Act is in need of renewal and appropriation which is predicted to be difficult. The ACC is looking to increase sponsorship for CPW. The Gabriella Miller Act was mentioned in the previous meeting minutes, but was not discussed.
- The Creating Hope Act had its first success with Biomarin and Vimizim.
- 21st Century Cures was mentioned. More information needs to be collected.

**Addressing Issues Interfering with Access to Care**

- As it is generally accepted that treating children on study is the standard of care, having more available clinical trials would reduce access problems. This is being attempted through the above funding and legislative tactics. The AAP has also re-initiated an effort to gain congressional support directed at the NIH to report the data on the inclusion of children in NIH trials.
- Access to investigational agents via compassionate use and expanded use mechanisms were discussed. Congressman McCaul is seeking input from stakeholders on legislation predicted to be drafted in 2015. This could include (but is not limited to) mandating publicly available criteria for inclusion, incentivizing policy, tracking and reporting mechanisms, and standardization of justifications for denial. The group felt that individual input would be best and the ACC will be available for comment after the draft is complete.
- Availability of FDA approved medication was identified as a risk area for access. Poor access could result from drug

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shortages, prior-authorization denials, medication cost, insurance coverage and tiered co-pays. The ACC did not agree this area was a priority for the group, but encouraged individuals interested to continue to work in this area outside of the alliance.

• Access to palliative/end-of-life care, supportive care, and survivorship care were identified as a concern for some members.

ACTION ITEMS

1. **Funding Follow-up:** A subgroup, selected by the ACC co-chairs, is organizing a meeting with NCI leadership to discuss opportunities to improve pediatric research funding. The proposed agenda includes discussion on transparency in criteria and process, future research goals, MATCH trial specifics, and suggestions for innovative opportunities.

2. **Develop Alliance Consensus:**
   - Complete governance structure to fill voids in leadership positions within ACC (events, communications and membership).
   - Agree on primary goals which will then trigger specific organizational considerations, identify constituents, allies and opponents, targets and tactics.

3. **Work Outside the Alliance:** Interested individuals will pursue independently or as smaller subgroups work in areas not addressed by the ACC, i.e. compassionate/expanded use, palliative care, payer relations.

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**Advocacy in Action**

### Grassroots Advocacy: AAP Key Contact Program

Key Contacts are AAP members who are interested in receiving advocacy opportunities and timely policy updates from the AAP Department of Federal Affairs on federal legislation and other issues important to the Academy.

Through regular e-mail communication with specific requests for action, the Department of Federal Affairs keeps Key Contacts informed of the latest legislative developments affecting children and pediatricians.

**How to Become a Key Contact:**

E-mail kids1st@aap.org with your name, AAP ID if known, and your preferred e-mail address. If you have questions about federal advocacy, contact AAP Department of Federal Affairs at 800-347-8600.

**FederalAdvocacy.aap.org: Dept. of Federal Affairs Online Resource Center**

Visit the AAP Department of Federal Affairs website at FederalAdvocacy.aap.org to find federal advocacy resources and tools, including:

• Contact and biographical information for your federal legislators
• An Action Center where you can call and e-mail federal legislators directly on current federal child health policy priorities
• Information on how to submit timely opinion pieces to local media outlets
• Fact sheets on health reform implementation and other timely topics
• All recent federal testimony given by AAP experts before the U.S. government on various child health topics
• Additional online resources such as PowerPoint presentations, videos, and other documents on current federal child health policy priorities.

**Save the Date: Legislative Conference 2015**

The AAP Legislative Conference will be held April 12-14, 2015, in Washington, DC. Participants will have the opportunity to develop their federal advocacy skills through interactive workshops, learn about timely child health policy topics, hear from several guest speakers from Congress and the Administration and visit with their legislators on Capitol Hill. If you are interested in attending and would like to be notified when registration opens, please email LegislativeConference@aap.org. For more information, please visit aap.org/legcon.
Liaison Updates

ACoS Commission on Cancer
Maria C. Velez, MD, FAAP
AAP SOHO Liaison

The Commission on Cancer (CoC) (https://www.facs.org/quality-programs/cancer/coc), a program of the American College of Surgeons (ACoS), recognizes cancer care programs for their commitment to providing comprehensive, high-quality, and multidisciplinary patient centered care. The CoC is dedicated to improving survival and quality of life for cancer patients through standard-setting, prevention, research, education, and the monitoring of comprehensive quality care.

As a member organization, the Academy has appointed me to represent pediatric oncology. In this position I typically attend two meetings per year and participate on many conference calls throughout the year in my role on two subcommittees.

At the May, 2014 meeting in Chicago, I was invited to join as a member of the Accreditation Committee as well as the Pediatric Oncology Measures Workgroup. This workgroup is revising the existing metrics for pediatric cancer programs that are accredited or seeking accreditation by the CoC. The emphasis of the workgroup is on Wilms Tumor and Neuroblastoma. The purpose and goal are to incorporate the same metrics as the COG staging system into the CoC. Conference calls were held in July, August, and October.

As a representative of the AAP SOHO, I was also invited to chair the Pediatric Oncology Standards Revision Workgroup. This workgroup is in charge of revising the CoC Standards for Pediatric Cancer Programs. Conference calls were held in June, August, and September. The workgroup reviewed the “Standards for Pediatric Cancer Centers” (http://pediatrics.aappublications.org/content/134/2/410.full.pdf) authored by the SOHO and published by the AAP in Pediatrics. The recommendations from that policy statement have been incorporated into the updated document. We are in the process of finalizing the first draft of the recommended revisions. Once the committee members agree on the recommendations, we will proceed to work in the specific details of the text.

Additional information regarding the CoC can be accessed through its newsletter at: http://newsmanager.commpartners.com/acscoc/issues/2014-11-03/email.html

Council on Pediatric Subspecialties Update

Gary Crouch, MD, FAAP
SOHO CoPS Representative

The Council of Pediatric Subspecialties advances child health through communication and collaboration within its network of pediatric subspecialties and liaison organizations. The highlight from the most recent CoPS newsletter is noted below. The full document, previous updates, and 2013-14 achievements can be accessed at: http://www.pedsubs.org/about/index.cfm

CoPS Recommends Delaying the Pediatric Fellowship Start Date

Who made the recommendation?

In October 2012, CoPS formed an Action Team (AT) to examine the current start date for fellowship training. The AT included representatives of categorical and fellowship program director organizations in pediatrics, surgery and internal medicine as well as Designated Institutional Officials (DIOs). The group held monthly conference calls to discuss issues and recommend solutions. In association with APPD, CoPS conducted two stakeholder surveys, one in June 2014 of pediatric residents entering fellowship (number of respondents=439) and the other in August 2014 of pediatric fellowship programs directors (n=495). After reviewing the results, the AT, with the approval of CoPS, made their recommendations.

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Why change the start date?
Graduating pediatric residents entering fellowship are expected to begin subspecialty training on July 1. As residency does not officially end until June 30, this can create conflict for those who must relocate and/or attend a mandatory orientation prior to July 1. In many programs, trainees utilize vacation to accommodate a move, but this is not always possible. The survey revealed that 69% of residents moved, usually with additional family, to another city for fellowship.

Thirty-nine percent were required to attend orientation before June 30. With increasing numbers of residents pursing fellowship and a fall match date, categorical program directors may have difficulty scheduling added time off for their residents finishing training. While the current system may work for fellowship program directors, residents and categorical program directors express significant concerns.

AAP Section on Surgery Liaison
Rebecka Meyers, MD, FAAP
AAP Section on Surgery Liaison

As part of an initiative to improve communication and relationships with subspecialists, the Section on Surgery (SoSu) has successfully instituted a liaison position with many other AAP committees and sections, sharing information about topics that are important to both groups. The Section on Surgery (SoSu) Liaison position on the SOHO Executive Committee was established in 2014 with the primary goals to:

• Provide a surgical perspective, when appropriate, on issues and activities
• Provide assistance/feedback in policy development and/or review
• Facilitate collaboration in education provided at the NCE
• Share information regarding SOHO activities and initiatives with the SoSu

As the new surgical liaison to the SOHO committee I would first like to thank the committee for their gracious and welcoming collaboration. I am member of the Executive Committee of the AAP Section on Surgery and Professor of Surgery at the University of Utah School of Medicine where I served as Chief of the Division of Pediatric Surgery from 2001-2011. My areas of expertise include hepatoblastoma and liver tumors, pediatric surgical oncology, pectus excavatum, and conjoined twins.

As we work together over the next few years I am hoping, in particular, to be able to work toward a joint collaborative education session at the fall meeting in 2016 or 2017. I am very much looking forward to working together with this committee. If any surgical issues come up outside of the formal committee structure with which you feel I might be able to offer some assistance please don't hesitate to contact me: Rebecka L Meyers: Rebecka.meyers@imail2.org; Professor of Pediatric Surgery; University of Utah School of Medicine; Salt Lake City, UT 84103.
Between 70,000 and 100,000 Americans are affected with sickle cell disease (SCD) and more than 2 million are estimated to have the heterozygous or homozygous sickle cell mutation. In the past few decades, the life span for patients with SCD has increased substantially with the vast majority entering adulthood; however, the overall life span continues to be shorter than the general population.

Patients with sickle cell disease can be afflicted with a multitude of acute and chronic medical issues affecting all major organ systems. Therefore, there is a clear need for evidence-based guidelines to dispense appropriate care to these patients.

Recently, updated guidelines from the National Heart and Lung Blood Institute (NHLBI) were published in an effort to address this need. The document was endorsed by many organizations including the AAP (http://pediatrics.aappublications.org/content/134/6/e1775.full.pdf+html) and is available at no cost on the NHLBI website at http://www.nhlbi.nih.gov/health-pro/guidelines/sickle-cell-disease-guidelines The executive summary is available at: http://jama.jamanetwork.com/article.aspx?articleid=1902235

An Expert Panel, co-Chaired by Drs. George Buchanan and Barbara Yawn, developed this report. Five major topic areas were identified to determine the areas that needed to be addressed. Literature searches were performed to answer the specific questions utilizing the PICOS methodology and GRADE system. The evidence underwent extensive review by the Panel and was subsequently graded on its quality. Evidence-based recommendations were synthesized and graded. If evidence was minimal, absent or inadequate, consensus statements were made based on the adaptations from other sources and/or the panel’s expertise.

The five topics covered by the guideline include health maintenance, management of acute and chronic conditions, use of hydroxyurea and blood transfusions in management of SCD. The guidelines are intended to be used by any practitioner who is involved in care of patients with SCD. Here we summarize some of the key recommendations from each of these areas.

1. Health Maintenance for People with Sickle Cell Disease
   a) Oral penicillin to be given twice daily for all patients with HbSS until 5 years of age. This may be discontinued at 5 years unless the patient had a splenectomy or an invasive pneumococcal infection. Recommendations were made to ensure that patients were adequately immunized against Streptococcus pneumoniae including boosters with PPSV23, and immunized against meningococcus.
   b) Annual screening for proteinuria with urinalysis is to begin at 10 years of age. If positive, orthostatic proteinuria should be ruled out before referral to a nephrologist.
   c) No recommendations for or against screening asymptomatic patients for pulmonary hypertension was made.
   d) Routine ECG screening was not recommended in asymptomatic children and adults with SCD.
   e) Adults and children with SCD were to be screened and treated for hypertension.
   f) Screening for sickle cell retinopathy to begin at 10 years of age.
   g) Patients with HbSS or HbSB⁺ (not HbSC or HbSB⁻) to be screened annually (from ages 2 to 16 years) with TCD for stroke prevention with actions based on results. Adults were not recommended to be screened with TCD. All asymptomatic patients were not recommended to be screened with MRI or CT.
   h) For pulmonary disease, while routine PFTs were not recommended in asymptomatic patients, screening by history and physical was recommended and evaluation was recommended for those with positive signs and symptoms of pulmonary disease.
   i) Several recommendations regarding reproductive care and contraception were also made.
2. Managing Acute Complications of Sickle Cell Disease
   a) Extensive recommendations were made regarding the most effective ways to manage vaso-occlusive crises (VOC). This included rapid assessment and treatment of VOC in a manner that is personalized to the patient’s needs. The intensity of pain management is to be escalated with the severity of pain symptoms, and with adequate monitoring and reassessment, the doses of opioids can be modified. Incentive spirometry and ambulation should be used to reduce the risk of secondary acute chest syndrome.

   b) Febrile illness should be promptly evaluated and treated. Febrile children should be treated empirically. If not ill, outpatient management with oral antibiotics can be considered, but those who appear sick or have high fevers should be hospitalized. Acute chest syndrome should be ruled out with a chest X-Ray in patients with lower respiratory signs and symptoms.

   c) Priapism should be intervened with ‘vigorous’ hydration, pain management and urology consultation.

   d) Hepato-biliary complications are to be managed depending on the specific issue. Acute cholecystitis is to be managed with antibiotics and surgical consultation. If cholecystectomy is needed, a laparoscopic approach is preferred and hematologist should be consulted for possible pre-operative transfusion. Asymptomatic gallstones should be monitored. Possible acute hepatic or intrahepatic crises are to be treated with hydration and close monitoring and, with a confirmed diagnosis by a hematologist, simple or exchange transfusion is the recommended treatment.

   e) In anemic episodes, the cause of the drop in hemoglobin from baseline should be investigated and CBC and reticulocyte count should be closely monitored. Symptoms of anemia and aplastic anemia should be managed with simple transfusions. Isolation procedures should be in place to prevent transmission of parvovirus B19 to high risk populations.

   f) Acute splenic sequestration should be managed with hydration and a sickle cell expert consultation for safe PRBC transfusion. Elective splenectomy after resolution of the acute episode can also be considered, with expert input.

   g) Acute chest syndrome should be ruled out in SCD patients who present with appropriate signs and symptoms of lower respiratory tract disease. If diagnosed, all patients with ACS should be hospitalized for monitoring and treatment; this should include IV cephalosporin, macrolide, supplemental oxygen if needed, incentive spirometry and simple transfusion. If a patient has worsening clinical course, exchange transfusion should be performed.

   h) SCD patients with neurologic signs and symptoms of an acute stroke should be evaluated urgently with radiologic imaging (non-contrast CT scan followed by MRI and MRA). Exchange transfusion should be performed if diagnosed. Following a stroke, all patients are to be transfused on a monthly basis, and if transfusion is not feasible, hydroxyurea should be started.

3. Managing Chronic Complications of Sickle Cell Disease
   a) The recommendations of management of chronic pain were mostly consensus-adapted. This includes the determination of the etiology of the pain, using a dedicated practitioner for the patient and an individualized treatment plan.

   b) Avascular necrosis should be ruled out in SCD patients with hip pain. If diagnosed, the pain should be managed with analgesics. Physical therapists and orthopedists with experience in such patients should be involved in the care to provide non-surgical and surgical treatments.

   c) Symptomatic patients suspected of pulmonary hypertension should have echocardiography, followed by right heart catheterization and treatment if the screening echocardiography (when not acutely ill) reveals an elevated TRV.

   d) Management of chronic renal disease (proteinuria, elevation of serum creatinine) in SCD should include consultation with a nephrologist, initiation of ACE inhibitor therapy and renal replacement therapy.

4. Hydroxyurea in the management of SCD
   In this section of the report, the Panel summarized the evidence to demonstrate and firmly establish the safety, tolerability and efficacy of hydroxyurea use in children and adults with SCD. Based on the evidence, several recommendations were made. Adults with HbSS or HbSB0 who have had multiple pain crisis, decreased quality of life from pain or anemia, or those with acute chest syndrome were to be prescribed hydroxyurea. All patients ‘regardless of clinical severity’ were to be offered hydroxyurea starting at 9 months of age. These were strongly recommended due to the quality of the evidence that supported it. A protocol for implementing the guidelines, including doses and

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monitoring parameters are also outlined.

5. Blood transfusion in the management of SCD

This section of the guidelines focused on the indications for PRBC transfusions (simple and exchange) in patients with SCD. This included acute and chronic conditions for which transfusions were recommended such as those undergoing procedures with general anesthesia, patients with acute chest syndrome, splenic sequestration, stroke (primary and secondary prevention), vaso-occlusive crisis, etc. Recommendations regarding optimal cross-matching methods (to reduce alloimmunization), goals of transfusion with regards to target hemoglobin and hemoglobin-S levels in acute and chronically transfused patients were also made. A consensus protocol for initiating and monitoring chronically transfused patients was included. Finally, complications from transfusions including alloimmunization, autoimmunization, iron overload, etc. were also discussed and recommendations to manage these complications were outlined.

The current report covers a wide range of issues related to the management of patients with SCD. It is an adequate tool for primary care providers and a good guide to the evidence basis for sickle cell care. Practitioners who are involved in the treatment of these patients will note that the panel made consensus recommendations in some areas of controversy. The report correctly suggests that additional good quality research is needed. There are still many other areas that are not addressed in the guidelines as new information is constantly emerging: 1. When to discuss transplantation with a patient and family and when to refer for consultation with a transplant team, 2. Screening and management of silent cerebral infarcts, 3. Neuro-psychologic function in children and adults, 4. The results of the yet to be published TWiTCH (TCD with transfusion in change to hydroxyurea) study and 5. Discussion of pulmonary hypertension guidelines from the American Thoracic Society for asymptomatic adults. Hopefully, these will be covered in the next version of this report.