Chair’s Update
Zora R. Rogers, MD, FAAP

Hello Fellow SOHO Members and Hello Spring!

Our SOHO Executive Committee (EC) elections have just concluded and I am pleased to share that Dr. Anne Warwick of the Uniformed Services University of the Health Sciences in Bethesda, MD was elected to a 3-year term on the EC. Drs. Cynthia Wetmore of The University of Arizona/Phoenix Children’s Hospital and Carl Allen of Baylor College of Medicine/Texas Children’s Hospital in Houston were re-elected to their second term on the committee. I look forward to working with all of you.

The work of the EC was also facilitated by the membership of Dr. Hope Wilson, now at The University of Alabama Birmingham, as the SOHO Training Fellow liaison. During her term on the EC, she established a trainee column in the SOHO newsletter, wrote an article for the Section on Pediatric Trainee newsletter about pursuing a career in pediatric hematology/oncology, developed and launched a survey of SOHO trainees which will be used to develop an engagement plan and participated in meetings and conference calls to provide insight from the perspective of a young physician regarding a variety of issues. Dr. Wilson’s term will end on June 30th and we will be reviewing the training fellow applications to fill that position.

And on that note, the work of SOHO depends on our volunteers. In addition to the Training Fellow liaison position, this fall we will be asking for volunteers for the joint AAP-ASPHO policy review committees we established several years ago (see pages 2-3 for details of this important partnership), serving on a SOHO subcommittee such as Communications (see the call for volunteers on page 11), and a new position as hematology payer liaison supporting the AAP’s staff as they engage insurance payers on behalf of the children and families we serve. (See the call for volunteers on page 8). Please consider volunteering now or in the future, SOHO needs you.

In the last few months, SOHO has participated in or commented upon 2 key issues:

- SOHO supported a sign on letter for Title VII Pediatric Subspecialty Loan Repayment – the AAP worked with other stakeholder organizations, including ASPHO to maintain this potential benefit for hematology/oncology subspecialists.
- SOHO was part of a valuation survey of the AAP Committee on Coding and Nomenclature (COCN) for revisions to the Office Visit Evaluation & Management

Continued on Page 2
(E/M) CPT codes in 2021. As many of you may know as part of the 2019 Medicare Physician Fee Schedule rule, the Centers for Medicare and Medicaid Services (CMS) proposed extensive changes to documentation and payment for E/M services, including applying a single payment rate for level 99212 through 99215 office visits. This clearly would negatively impact Hematology/Oncology E/M services due to the complexity of the conditions we treat. Comments by many organized medicine organizations, including the AAP, called on CMS to postpone implementation of the payment collapse pending further efforts by the CPT Editorial Panel and the AMA/Specialty Society RVS Update Committee (RUC) to develop a new coding structure. As Joint CPT-RUC Workgroup on E/M was recently formed to develop a coding proposal. The AAP is one of only several medical specialty societies participating in this RUC survey. The COCN selected a random sample, including the SOHO membership, in order to keep the survey pool manageable. If you were chosen and participated – thank you!

Our SOHO and ASPHO policy review partnership remains a robust way to ensure one voice for pediatric hematology/oncology on the national stage. These volunteers review new guidelines, policies, AAP manual chapters, that pertain to pediatric hematology/oncology. Again, please see the article below to learn more about the progress of this collaboration. New members for open positions on the review committees will be selected in later 2019. We also have policies on treatment of iron deficiency, long term follow-up care for pediatric cancer survivors, and health supervision of children with sickle cell anemia (guidance for the general pediatrician) in various stages of development. Thank you also to the authors of these documents for their generous volunteering of their time and expertise.

Another product of our engaged and passionate members is the recently published AAP clinical practice guideline, Clinical Practice Guideline for the Management of Infantile Hemangiomas, for which Dr. Francine Blei, served as the SOHO and ASPHO representative. I would like to extend our appreciation to Dr. Blei for her role in the development of this important guideline.

Lastly, an issue of importance to physicians who care for patients with sickle cell disease has been addressed by CMS as a result of advocacy from many stakeholders. On April 1, 2019 CMS released the final Part D Call Letter. In the second paragraph on page 218, CMS recommended that “beneficiaries with SCD be excluded from the opioid safety edits. The CDC Guideline for Prescribing Opioids for Chronic Pain stated that “given the challenges of managing the painful complications of sickle cell disease, readers are referred to the NIH National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for management of sickle cell disease.” You can review the entire document here.

SOHO continues to make an impact on the management of children and families with blood disorders and cancer. It is only with your continued support and involvement that this is possible. To all of our current and former volunteers an enormous thank you! If you have not yet become involved please consider doing so this next year! As always I appreciate your comments on how we can increase the value of your membership in SOHO.

Sincerely,

Zora R. Rogers, MD, FAAP, Chairperson
Section on Hematology/Oncology

---

**SOHO/ASPHO Collaborative Policy Process Update**

The AAP Section on Hematology/Oncology (SOHO) and the American Society of Pediatric Hematology/Oncology (ASPHO) developed and implemented a collaborative policy review process in January 2014. The overarching goal of the process is to provide pediatric hematology/oncology (PHO) review expertise regarding policy and other documents for physicians who care for children with blood disorders and cancer. This process addresses two general areas.

The first is the review of policies and guidelines from other AAP sections, councils and committees as well as, at times, from other medical societies. SOHO and ASPHO established the following 11 review groups that engage 52 members of our organizations:

Continued on Page 3
SOHO/ASPHO Collaborative Policy Process Update  Continued from Page 2

• Solid tumors
• Benign hematology
• Leukemia/lymphomas/lymphoproliferative disorders
• Health care delivery and health policy
• Coagulation disorders
• Hemoglobinopathies
• Stem cell transplantation
• Oncology supportive care
• Neuro-oncology
• Transfusion
• Survivorship and late effects

Their review and feedback help to reinforce the voice of PHO specialists as it pertains to statements developed by internal AAP as well as external groups. Since inception, the policy review groups have reviewed over 164 policy statements, clinical practice guidelines, book chapters and other documents from the AAP and other societies. Thank you to all who volunteer and have supported this effort over the past 5+ years! A list of the review group volunteers can be seen on the SOHO Collaboration Site here.

The second area is the development of policies that address PHO-related conditions and issues. As part of the technical review process, draft policy is reviewed by the appropriate PHO review group/s along with many groups within the AAP who provide feedback to the authors. Below is a list of current policies that have been developed, are under revision or are in the process of initial development by SOHO and some in collaboration with other AAP groups:

• Preservation of Fertility in Pediatric & Adolescent Patients with Cancer (under revision)
• Cord Blood Banking for Potential Future Transplantation (under revision)
• Standards for Pediatric Cancer Centers (revision)

Policies that are a collaboration with ASPHO:

• Supervision of Children with Sickle Cell Disease (under revision)
• Treatment of Iron Deficiency Anemia in Infants, Children and Adolescents (new clinical report in process)
• Long-term Follow-up Care for Pediatric Cancer Survivors (also in collaboration with the Children's Oncology Group; under revision)
• Evaluation for Bleeding Disorders in Suspected Child Abuse and Evaluating for Suspected Child Abuse: Conditions That Predispose to Bleeding (also in collaboration with the AAP Committee on Child Abuse (under revision)

There is also PHO representation on two clinical practice guidelines developed/under development by the AAP:

• Clinical Practice Guideline for the Management of Infantile Hemangiomas
• Clinical Practice Guideline on Hyperbilirubinemia

This important work guides clinical practice for countless pediatric providers nationally and internationally. We are very appreciative of the authors who continue to volunteer their time and expertise to support the policy development process. Watch for future opportunities to serve on the policy review groups fall 2019.

AAP Academic and Subspecialty Advocacy Report
and Subspecialty Advocacy Toolkit

The latest AAP Academic and Subspecialty Advocacy Washington Report is now available! The report contains a special welcome message from AAP President, Dr. Kyle Yasuda and details the important advocacy work that the Academy is engaging in, highlighting issues of particular importance to medical and surgical subspecialty pediatricians. The

Continued on Page 4
report includes updates on AAP advocacy efforts to support Medicaid, prevent firearm-related injury and death, protect immigrant children, promote pediatric subspecialty workforce issues, and increase funding for pediatric research, among many other issues.

We are also excited to announce the release of the AAP Subspecialty Advocacy Toolkit. This toolkit provides information on ways for subspecialists to engage in advocacy across all levels of government with the support of the AAP's advocacy team. We hope you find this to be a helpful resource and look forward to hearing from you about ways we can continue to improve this tool. Please contact Suzanne Kirkwood at skirkwood@aap.org with any comments or questions.

Thank you for all you are doing for children and families!

Training Fellow Liaison Column:
Seeking a Job in Pediatric Hematology/Oncology (PHO)

Hope P. Wilson, MD, FAAP
SOHO Training Fellow Liaison
University of Alabama at Birmingham

The moment you have dreamed of is finally here. Now what? Where is the nice checklist of things to do? What about the list of commonly asked interview questions? This time is different, very different from residency and fellowship and to complicate things even more there's no rank list or match. Will I find a job? These are a few of the many questions that ran through my mind as I embarked on the search for my first “real job”.

As you approach the end of your fellowship training, the most important thing to do is take time to think through and define your career goals. A few essential questions to ponder when pursuing a job in PHO are whether you want to practice hematology, oncology, or both? Do you want to practice in an academic or private setting? If academic, are you most interested in a clinical or research position?

Inevitably, you will be asked “Where do see yourself in the next 5 years?” So, it behooves you to have already put thought into this, not just to be able to provide a well-polished answer but more importantly so that you can critically appraise each job opportunity to ensure it aligns with your ultimate career plan.

Now that you have established that, it’s time to start exploring to see what’s out there. The following sites have PHO job postings and are a good resource: AAP Career Center-Peds Jobs ASPHO Career Center, ASH Job Center, Indeed and when all else fails, you can always count on the infamous Google. Additionally, individual programs may have available jobs posted on their respective websites. Do not be discouraged if the listings are few. I found that the majority of jobs were not posted. This is where networking at meetings and conferences is invaluable as you may learn of potential job opportunities. It is never too early to network!

The next step is to update your curriculum vitae (CV) and prepare a cover letter, which is a summary of your training experiences and career plan, highlighting why you are the best candidate for the job. Have your mentor and other faculty members at your program review both and provide constructive feedback to make it the best. You can start sending these out as early as the fall of your final year of fellowship. When there is an actual listing, tailor your cover letter focusing on your skills that align with what they are recruiting for. These documents should be sent to the contact provided in the ad, which often times is a recruiter. Otherwise, you should send inquiries to the leadership of the program of interest, most commonly the Division Chief. Apply for jobs even if at first glance, they may not seem to be what you are looking for. Do not rule out an opportunity until you have interviewed, as the job description may be flexible. In other words, do not judge a book by its cover.

In preparation for the interview, research the program to have some basis for your interview. This shows your interest and initiative, which definitely helps make for a less awkward Q & A style interview as opposed to a genuine conversation. For academic programs, be prepared to give a presentation or “chalk talk”, most often on your fellowship research or about
other interesting projects from your CV.

To put all of this into perspective, I began sending out inquiries in September of my 3rd year of fellowship. I applied to 14 programs and received responses from all but 2. Unfortunately, the majority of those responses were that they were not currently recruiting but that they would keep my CV on file in the event of an opening. Ultimately, I interviewed at 4 programs, ranging from private to academic, small to large size. After much thought and reflection on my career goals, I narrowed it down to 2 programs and finally accepted an Assistant Professor position in May (yes May!) at the University of Alabama at Birmingham, which ironically was the only one of the 4 places that didn't have a job posting.

As I reflect, the best advice I can give is to trust the process. Be calm, be confident, and most importantly be you.

Here are additional resources provided by the American Academy of Pediatrics that may be helpful as you navigate the transition from fellowship into the workforce.

- Managing Medical School Debt
- Career Support
- Early Career Decisions-Salary
- Negotiating Employment Contracts

AAP Mentorship Program - Employment Contracts: Things to consider (Available on the AAP Mentorship Program Forum) – Get insight on details you should expect when a job offer and contract are presented to you. This informative discussion forum is presented within the AAP Mentorship Program. If you aren't a part of this online mentorship community, you should be! Whether you need a small amount of mentorship quickly (flash mentoring) or a long-term mentorship connection, the AAP Mentorship Program has you covered. The AAP Mentorship Program is free to all AAP members.

I am happy to answer any additional questions that you may have. I can be reached at hwilson@peds.uab.edu.

---

**Clot prevention at a Children’s Hospital: Instituting a Pediatric Thromboprophylaxis Protocol in a Tertiary-Care Pediatric Center**

Jayson Stoffman, MD, FRCPC, FAAP
Associate Professor and
Director, Pediatric Post-Graduate Medical Education
Section of Pediatric Hematology/Oncology/BMT
Department of Pediatrics and Child Health, University of Manitoba

*Venous thromboembolic events (VTE) are relatively uncommon in pediatrics, with Canadian registry data suggesting an incidence of around 0.07 per 10,000 children or 5.3 per 10,000 pediatric hospital admissions. However, the rate of VTE in hospitalized children is increasing, most likely a reflection of the increased acuity of illness and the increasing use of indwelling vascular lines. These acquired risk factors for thrombosis often occur in conjunction, which further increases the likelihood of a thrombotic complication during hospitalization. In the adult literature, there is good evidence for the use of thromboprophylaxis, both mechanical and pharmacological, but the corresponding data in pediatrics is lacking.*

*As a general strategic approach in the adult literature, all medical and surgical patients require thrombotic risk assessment and should be considered for prophylaxis. Patients who are particularly at risk are those with prolonged hospitalization, reduced mobility, heart or respiratory failure, acute infection or inflammatory illness, or cancers. In those at-risk patients, heparins were traditionally considered effective pharmacological prophylaxis, with a preference for the low-molecular-weight heparins for ease of administration and dosing. The advent of the direct oral anticoagulants is changing the approach to thromboprophylaxis in adults, as these agents are demonstrating equivalent efficacy and safety with even simpler administration. Mechanical prophylaxis should also be considered for all patients.*

*Continued on Page 6*
Despite increasing interest in the development of clinical guidelines for pediatric anticoagulation, the issue of thromboprophylaxis is not well evaluated. The 2012 Chest guidelines on pediatric anticoagulation generally confines the discussion of prophylaxis to central vascular access devices and specific indications such as total parenteral nutrition and Kawasaki disease. The more recent 2018 guidelines from the American Society of Hematology are focused on therapeutic anticoagulation, with the comment that future guidelines should consider prophylactic use.

In pediatrics, there is more variability in use of pharmacological thromboprophylaxis. Adolescents are generally more likely to receive thromboprophylaxis, but still at a lower rate than adults. In general, prophylaxis patterns in children reflect the recognized risk factors for VTE, but a lack of evidence of risk and benefits of thromboprophylaxis and misconceptions of the burden of illness of VTE in children and adolescents limits their uptake. At Children's Hospital of Philadelphia, a quality improvement initiative was started after a noted increased incidence of hospital-acquired VTE. Their thromboprophylaxis algorithm was developed by consensus opinion, with the final treatment decision left to the discretion of the primary physician. The guidelines were promoted and implemented with active compliance measures and follow-up; this did not reveal an increase in the amount of anticoagulation prescribed but did reveal an increased appreciation of the risk of thrombosis, particularly among nursing staff.

The Children's Hospital, Health Sciences Centre in Winnipeg, Manitoba is the primary pediatric hospital for the province of Manitoba with 127 beds, including a Pediatric ICU and Level 4 Neonatal ICU. All anticoagulation for in-patients requires consultations with the Pediatric Hematology service. There was an interest from both the surgical and intensive care services and the Pediatric Hematologists in developing a process for prophylactic anticoagulation that would not require this direct involvement of Hematology while still being appropriate and safe. The guidelines developed at CHOP were taken as a baseline for modification to the specific needs of our center and population.

Development of the thromboprophylaxis guidelines was initiated as a quality improvement initiative, and a working group was assembled under the Child Health Quality Team. The group included representation from Pediatric Hematology, Orthopedic and General Surgery, Intensive Care, Physiotherapy, Occupational Therapy, Nursing, and Quality. Initial meetings established the need for the guidelines and the available supporting evidence, which was admittedly limited. From the CHOP guidelines, an algorithm was developed by group consensus which incorporated the risk of development of VTE and the risk of complications from anticoagulation. The working group also felt it was important to include mechanical as well as pharmacologic measures.

During the development of the guidelines, there were frequent meetings of the working group, whose members reviewed the interval drafts within their individual medical and allied health groups for their input. The Quality Team also engaged other groups likely to be impacted, such as Anesthesia. Those discussions were particularly helpful in defining absolute and relative contraindications to prophylactic anticoagulation. The final versions were taken under review by the hospital's clinical program management team, and ultimately by the administrative leadership for final approval.

**ASH Guidelines on SCD Available for Public Comment**

The American Society of Hematology (ASH) is seeking comments on two draft clinical practice guidelines on sickle cell disease (SCD): pain and transplantation. Materials will be available through May 13th and can be found at [www.hematology.org/Guidelines-Public-Comment](http://www.hematology.org/Guidelines-Public-Comment). These are the fourth and the fifth of five forthcoming guidelines on SCD. Anyone is welcome to review the draft recommendations and submit comments, including ASH members, non-member physicians and researchers, allied professionals, representatives of medical societies, industry and insurance companies, patients, caregivers, and members of the public. Feedback received will be provided to the guideline panels for review. Comments will also be considered for implementation and dissemination efforts following publication, and future revision efforts. Please let your colleagues and friends know about this public comment period.
The final algorithm is shown in the figure, and a formal institutional policy and standard order set were created. It starts with the decision on whether or not the patient is able to ambulate; if so, mobilization is encouraged. Those who are unable to mobilize and aged greater than 14 years are evaluated for established risk factors for thrombosis, including acute trauma, obesity, presence of a central venous catheter, and chronic inflammatory conditions. Where a risk factor is present, contraindications to anticoagulation are assessed, such as active bleeding or coagulopathy or anticipated surgical intervention in the immediate future. In the absence of risk factors, pharmacologic prophylaxis is recommended. The requirement for approval for thromboprophylaxis by Hematology was waived for those patients meeting the recommendation for anticoagulation. Guidance was also provided for those patients who did not qualify, including the consideration of Hematology consultation for anticoagulation outside of the guidelines.

For patients without a risk factor for thrombosis or those with contraindications to anticoagulation, early mobilization and mechanical thromboprophylaxis with graduated compression stockings are encouraged, and these measures are also recommended when anticoagulation is given. For patients younger than 14 years, where the evidence for prophylactic anticoagulant was most limited, mechanical prophylaxis and Hematology consultation are recommended when two or more risk factors for thrombosis are present. Other children excluded from the guidelines are those with known abnormalities of coagulation, neonatal patients, patients with significant cardiac conditions, solid organ transplant recipients, patients on hemodialysis, and those with a history of stroke; Hematology consultation was recommended where prophylactic anticoagulation was being considered outside of the guideline.

Following the approval of the policy and standard order set, nursing education was carried out on the key impacted wards.

Permission to publish this Algorithm was provided by the Winnipeg Health Sciences Centre.

Permission to publish this Algorithm was provided by the Winnipeg Health Sciences Centre.
and information also provided to the hospital attending staff and residents in Pediatrics, Intensive Care, and the surgical specialties. The algorithm and order set were made available on all the wards in an accessible location. While awareness of the guidelines was very high following their initial introduction, it did wane over the subsequent months, and was significantly affected by the turnover in house staff, particularly surgical residents on their Pediatrics rotation. Fortunately, nursing support remains strong, and appreciation of the patients at risk of thrombosis and the need for monitoring, mobilization, and mechanical measures is proactively considered. Where pharmacological thromboprophylaxis is necessary, the process for obtaining anticoagulation is much smoother.

While there were plans to audit the guidelines as part of ongoing quality improvement, this part of the initiative has unfortunately not yet taken place. Still, our experience shows the value in developing a specific policy for pediatric thromboprophylaxis which is adapted to the unique needs and abilities of the individual center.

References:

CoPS Update

Dr. Cynthia Wetmore serves as the AAP Section on Hematology/Oncology Liaison to the Council on Pediatric Subspecialties (CoPS). You can view the minutes from the fall 2018 meeting and additional information about CoPS on their website.

Call for Nominations – SOHO Payer Advocacy Contact - Hematology

Background:
The mission of the Section on Hematology/Oncology (SOHO) is to educate the pediatric practice community and families regarding pediatric hematology/oncology conditions, make recommendations about health care needs of these patients, and advocate for those who provide and require the care.

The SOHO Payer Advocacy (PA) Contact positions (one to address hematology and one to address oncology-related issues) were established to support PA activities and issues related to care for pediatric PHO patients and payment of PHO pediatricians.

Liaison Responsibilities:
The responsibilities of a payer advocate would be:
1. Interface as necessary with AAP Payer Advocacy Advisory Committee (PAAC) and payer advocacy as the SOHO contact regarding payer issues. This may include occasional conference calls.
2. Convey to PAAC any payer issues identified by SOHO and its members
3. Educate SOHO members regarding existing payer advocacy resources (i.e., the hassle factor form to report payer issues and the Practice Transformation site).
4. Explore additional resources that may assist SOHO members in future payer issues (i.e., develop new and/or request current letters used by SOHO members regarding specific types of payer issues).
Call for Nominations . . . Continued from Page 8

5. Educate SOHO members regarding current PAAC activities by sharing the PAAC Scorecard through articles in the SOHO newsletter and e-updates.

6. Explore ways to educate SOHO members about how to approach issues with private payers regarding pre-authorization and other coverage issues related to care of PHO patients (i.e., key talking points, engaging their state AAP chapter, when/how to escalate an issue to a higher level).

7. Facilitate review of carrier coverage and payment policies as they relate to hematology and oncology

Ideally, candidates would have an understanding of health insurance including managed care, payer contracting, in addition to coding. Ability to both see the ‘big picture’ in child health financing as well as be detail-oriented and have a balanced approach when dealing with potentially contentious issues involving payment.

Eligibility:
- Member of the American Academy of Pediatrics
- Member of the Section on Hematology/Oncology

Term: 3 years; renewable subject to Executive Committee approval

Appointment Criteria for Consideration by Executive Committee:
- Letter/email of Interest from the SOHO Member
- Curriculum vitae

Status: Members appointed by the SOHO Executive Committee

If you are interested in submitting your nomination to be considered for either the hematology or oncology position, please send the above information to skirkwood@aap.org by Friday, May 17th.

Call for Input:

Payer Policies on Advanced Radiologic Imaging Procedures

The American Academy of Pediatrics would like to hear from you regarding your experience with payer policies on advanced radiologic imaging procedures. Some insurance companies are steering pediatric patients (10 years of age or older) away from hospital-based outpatient imaging centers (e.g. at pediatric hospitals) toward less expensive free-standing (non-hospital) imaging centers. They use age cut-offs and other criteria to determine whether patients’ medical needs warrant imaging at a dedicated pediatric center. An example of a carrier policy that AAP Members have expressed concerns with can be viewed here.

We encourage you to take a few minutes to complete this survey by Wednesday, May 15, 2019, providing as much detail as possible, if you have experienced an issue with quality/safety of imaging or delayed diagnoses as a result of carrier imaging policies.

Hot Papers in Pediatric Hematology/Oncology

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


Investigators from St. Jude Children's Research Hospital analyzed whole-genome sequencing

Continued on Page 10
from 1,133 female childhood cancer survivors (median age at last follow-up 35.4 years; range, 8.4–67.4), for germline mutations in 170 common breast cancer predisposition gene variants. In this cohort, there were 47 diagnosed with one or more subsequent breast cancers (median age at subsequent breast cancer 40.3 years; range, 24.5–53.0). Included breast cancer predisposition genes were *BRCA1*, *BRCA2*, *TP53, PTEN, CDH1, STK11, NFI, PALB2, ATM, CHEK2*, and *NBN*. A polygenic risk score (PRS) was calculated as a weighted sum of the number of risk alleles carried by an individual, in which their weights were taken as the natural logarithm of the previously published meta-analysis-estimated odds ratios of the corresponding loci. Adjusting for attained age, age at primary diagnosis, chest irradiation, doses of alkylating agents and anthracyclines, and genotype eigenvectors, relative risks (RRs) for all survivors with PRS in the highest versus lowest quintiles were 2.7 (95% CI, 1.0–7.3), for survivors with chest irradiation 3.0 (95% CI, 1.1–8.1), and for survivors without chest radiation 2.4 (95% CI, 0.1–81.1). Overall, the PRS was associated with subsequent breast cancer under the age of 45 years with a RR 3.2 (95% CI, 1.2–8.3). This PRS may help to identify high-risk survivors for surveillance and potential prevention of subsequent breast cancer.


Other investigators from St. Jude Children's Research Hospital analyzed results from three-platform whole genome (WGS), whole exome (WES), and transcriptome (RNA-Seq) sequencing of paired tumor and normal tissue from 78 pediatric cancer patients to improve clinically relevant accuracy and time to results. Their three-platform sequencing had a positive predictive value for somatic single nucleotide variations of 97–99%, for small insertion-deletions of 99%, and for structural variants of 91% based on independent experimental verification of 15,225 variants. Compared to the 78% sensitivity of current standard WES and RNA-Seq testing only, by adding WGS they discovered 240 pathogenic variants across all cases, including 84 of 86 known from previous diagnostic testing for 98% sensitivity. In the clinical setting, three-platform sequencing achieved a median turnaround time of 31 days from sample receipt to report which they found comparable to two recent clinical genomic studies using other techniques. The disadvantages of three-platform sequencing were the large computing infrastructure required for data storage and analysis, and the cost of sequencing.


Investigators from the Shanghai Jiao Tong University School of Medicine performed comprehensive variant analysis by next-generation sequencing in 111 pediatric patients morphologically diagnosed as acute promyelocytic leukemia (APL) but who had inconclusive karyotype analysis, FISH, and RT-PCR. Structural variant (SV) analysis in 120 DNA samples from both diagnosis and relapse identified 95 samples with *RARA* rearrangement (including 94 with PML-RARA and one with NPM-RARA) and two samples with *KMT2A* rearrangement. In the eligible 13 RNA samples without any RARA rearrangement at diagnosis, one case each with *CPSF6-RARG, NPM1-CCDC28A*, and *TBC1D15-RAB21* and two cases with a *TBL1XR1-RARB* fusion were discovered. These uncovered fusion genes strongly suggested their contributions to leukemogenesis as driver alternations and APL phenotype may arise by abnormalities of other members of the nuclear receptor superfamily involved in retinoid signaling (RARB or RARG) or even by mechanisms distinct from the formation of aberrant retinoid receptors.

Single-nucleotide variant (SNV) analysis in 77 children (80 samples) with RARA rearrangement showed recurrent alternations of primary APL in *FLT3, WT1, USP9X, NRAS, and ARID1A*, with a strong potential for involvement in pathogenesis, and *WT1* as the only recurrently mutated gene in relapsed APL. *WT1, NPM1, NRAS, FLT3*, and *NSD1* were identified as recurrently mutated in 17 primary samples without RARA rearrangement and *WT1, NPM1, TP53*, and *RARA* as recurrently mutated in 9 relapsed samples. The survival of APL with RARA rearrangement was better (estimated 5- and 8-year OS was 96.1 ± 2.1%, ) than without RARA rearrangement (estimated 5-year and 8-year OS rates were 85.0 ± 10.2% and 63.8 ± 19.9%, respectively). Thus, patients morphologically diagnosed as APL that cannot be identified as having a RARA rearrangement may be considered as a subclass of AML rather than APL, with individualized treatment given accordingly.


Continued on Page 11
Investigators from multiple US institutions led by Memorial Sloan Kettering Cancer Center, performed whole-genome DNA, and transcriptome RNA and miRNA sequencing analysis of bone marrow myeloblasts and fibroblasts obtained at diagnosis, pre- and post- induction failure on 28 children with pediatric AML enrolled in COG protocol AAML0531. They identified at least three genetic groups of patients with induction failure, including those with NUP98 rearrangements, somatic mutations of WT1 in the absence of apparent NUP98 mutations, and additional recurrent variants including those in KMT2C and MLLT10. While exhibiting overt therapy resistance, these leukemias nonetheless showed diverse forms of clonal evolution upon chemotherapy exposure. This included selection for mutant alleles of FRMD8, DHX32, PIK3R1, SHANK3, MBLN1, as well as persistence of WT1 and TP53 mutant clones, and elimination of FLT3, PTPN11, and NRAS mutant clones. Primary chemotherapy resistance in pediatric AML seems to depend on various genetic changes based on unique mutation combinations which could guide future studies to improve diagnosis and subsequent therapy targets.


Multiple institutions led by investigators from St. Jude Children’s Research Hospital used integrated genomic analysis (WGS, WES, SNP) of 1,988 marrow samples from children and adult with B-ALL, to devise a new taxonomy of B-ALL incorporating 23 subtypes defined by chromosomal rearrangements, sequence mutations, or heterogeneous genomic alterations, with varying frequency according to age. Twelve previously recognized subtypes accounted for 75.8% of the cohort including high hyperdiploidy (14.0%), low hypodiploidy (3.9%), near haploidy (1.5%) and intrachromosomal amplification of chromosome 21 (iAMP21; 3.2% of 1,141 cases with SNP array data). Notably, the gene expression profile of near haploid B-ALL was similar to that of high hyperdiploid ALL, suggesting a common pathogenesis. Subtypes defined by rearrangements or gene expression profile include BCRABL1 (Ph; 6.2%), Ph-like (18.1%), ETV6-RUNXI (9.4%), KMT2A (MLL)-rearranged (KMT2A; 6.8%), DUX4-rearranged (DUX4; 5.3%), TCF3-PBX1 (3.9%), ZNF384-rearranged (ZNF384; 2.5%) and MEF2D-rearranged (MEF2D; 2.2%). There was marked variation in the prevalence of subtypes according to age, with ETV6-RUNXI and high hyperdiploid ALL being most common in children, and low hypodiploid, KMT2A and kinase-activated (Ph and Ph-like) ALL being more common in adults.

Two subtypes had frequent alterations of the B lymphoid transcription-factor gene PAX5. One, PAX5alt (7.4%), had diverse PAX5 alterations (rearrangements, intragenic amplifications or mutations). Children in this subtype were more commonly classified as high risk (n = 63) rather than standard risk (n = 17). A second subtype is defined by PAX5 p.Pro80Arg and biallelic PAX5 alterations. In children treated in the Children's Oncology Group AALL0232, the outcome was intermediate for both PAX5 p.Pro80Arg (5-year event-free survival (EFS) 75.0 ± 14.2%, overall survival (OS) 75.0 ± 14.2%, eight evaluable cases) and PAX5alt (EFS 71.5 ± 7.0%, OS 75.7 ± 6.6%, 46 evaluable cases) compared with DUX4 ALL and other favorable risk subtypes (high hyperdiploid, ETV6-RUNXI and TCF3-PBX1). In contrast, the outcome for PAX5 p.Pro80Arg in children treated on St. Jude Total Therapy protocols was unfavorable, although few subjects were evaluable and were treated on multiple protocols. These results demonstrate the utility of transcriptome sequencing to classify B-ALL and reinforce the central role of PAX5 as a checkpoint in B lymphoid maturation and leukemogenesis.

Call for Volunteers: Communications Subcommittee Positions

The SOHO Communications Subcommittee is responsible for the Section newsletter and website and oversees information shared regarding Academy and pediatric hematology/oncology related information with Section members.

The Communications Subcommittee is responsible to work with the Subcommittee Chair to:

- Recommend topics/themes for the newsletter.
- Write and/or recommend authors for newsletter content. Contact potential authors for submitting articles, as necessary.
- Develop mechanisms to solicit feedback from Section members to further inform the direction and focus of the newsletter.
- Review of the website and identifies gaps or needed updates.
Call for Volunteers: Communications Subcommittee Positions

Continued from Page 11

- Recommend topics/themes for the website and prepare original content.
- Provides insights on the collection of feedback from the Section members and website analytics to further inform the direction and focus of the website.
- Participate in periodic planning conference calls, as necessary.

At this time, we are seeking volunteers to serve a three-year term on the Subcommittee. For additional information please refer to the position description here. If you are interested, please submit your CV and letter of interest to Suzanne Kirkwood at skirkwood@aap.org by May 17, 2019.

---

2019 Coding and Reimbursement Tip Sheet for Transition from Pediatric to Adult Health Care

In 2018, the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Physicians published an updated clinical report on transition that represents expert opinion and consensus on practice-based implementation of transition for all youth, beginning early in adolescence and continuing through young adulthood. This updated clinical report calls for a structured transition process based on the Six Core Elements of Health Care Transition™, which can be customized for use in a variety of primary and specialty care settings and are available at no cost from Got Transition™, the national resource center on health care transition (www.GotTransition.org).

To support the delivery of recommended transition services in pediatric and adult care settings, Got Transition and the American Academy of Pediatrics partnered to develop and update each year this transition payment tip sheet. It begins with a listing of transition-related CPT codes and corresponding Medicare fees and relative value units (RVUs), effective as of 2019. It also includes a set of clinical vignettes with recommended CPT and ICD coding and CPT coding descriptions for transition-related services with selected coding tips. A supplemental table (Appendix A) categorizes these codes based on the type of providers able to report them and whether the service can be delivered face-to-face or non-face-to-face. Also included in this tip sheet is a letter template that can be customized and sent to payers calling for recognition of transition-related CPT codes (available here and in Appendix B).

Additional transition payment strategies are available in a 2018 report, Recommendations for Transition Value-Based Payment for Pediatric and Adult Health Care Systems. This report includes the recommendations of key stakeholders representing Medicaid and commercial payers, health plans/accountable care organizations, employers, health professional organizations, and family advocacy groups. A prioritized set of value-based payment options are presented with examples for their potential use, including enhanced fee-for-service payments, infrastructure investments, pay-for-performance payments, direct payments to consumers, episode of care or bundled payments, and per member per month payments. In addition, this report includes a set of prioritized quality measures that can be used with the value-based payment options. View the full resource here.

Tech Tip

Although not just for pediatric hematology/oncology, Readability.VisibleThread.com is a tech tool to improve your writing. It analyzes text using algorithms to check readability level and compliance risks. Use it to improve your informed consents and your community engagement letters. This is a free feature of a commercial software, but an account needs to be established to utilize.

*Inclusion of this information within this communication does not represent endorsement of the product by the AAP or the Section on Hematology/Oncology, but is being shared as an information only.
New: SOHO Collaboration Site!

As a member of the AAP Section on Hematology/Oncology (SOHO) you have access to the SOHO Collaboration Web site. This member's only benefit of the SOHO grants each current Section member access to the following:

Opportunities to get involved in the SOHO leadership committees and policy review groups.
Information for trainees regarding a career in pediatric hematology/oncology.
Section publications including the newsletter and AAP News articles.
Quick access to new and/or existing AAP policies developed by SOHO and practice guidelines of interest to SOHO members.

And much more!

View Access Instructions below. For questions or suggestions regarding the SOHO collaboration site please contact SOHO Staff, Suzanne Kirkwood or the SOHO Chair, Dr Zora R. Rogers.

Step 1: Visit http://www.aap.org click on “My Collaboration Sites” at the top of the webpage.
Step 2: Log in with your AAP login credentials.
Step 3: Access your Section collaboration site
Step 4: Begin navigating your site. Note- You can bookmark your site for future use
Sickle Cell Disease Coalition (SCDC) Update

The mission of the SCDC is to amplify the voice of the SCD stakeholder community as well as promote awareness and improve outcomes for individuals with SCD. The Coalition will focus on promoting research, clinical care, education, training, and advocacy. The SCDC will serve as a platform to encourage stakeholders to work together to develop and implement important projects and activities that will ultimately help to improve outcomes for individuals with SCD.

The AAP is a member of the SCDC and SOHO Chair, Dr. Zora Rogers and AAP SOHO Manager, Ms. Suzanne Kirkwood, currently serve as the representatives.

Previous issues of the SCDC Update and a subscription form to the e-newsletter are available here on the SCDC Coalition website. We encourage you to share this information with your colleagues who have an interest in sickle cell disease.

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 the AAP website membership page. Thank you to all who have continued to support the AAP and the Section by renewing their memberships. And welcome to new members of the Academy and the Section!

For Upcoming Newsletters . . .

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

The Section on
Hematology/Oncology
Executive Committee

Chairperson:
Zora R. Rogers, MD, FAAP

Executive Committee:
Carl Allen, MD, PhD, FAAP
James Harper, MD, FAAP
Jeffrey Lipton, MD, PhD, FAAP
Cynthia Wetmore, MD, PhD, FAAP
Hope Wilson, MD, FAAP – Training
Amber Yates, MD, FAAP

Immediate Past-Chair:
Jeffrey Hord, MD, FAAP

Fellow Liaison

Liaisons:
David Dickens, MD, FAAP
Alliance for Childhood Cancer
Maria Velez, MD, FAAP
Commission on Cancer
Cynthia Wetmore, MD, PhD, FAAP

Council on Pediatric Subspecialties

Staff:
Suzanne Kirkwood, MS
Manager, Section on Hematology/Oncology

Journal Production Specialist
Mark A. Krajecki

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.