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Short Communication

Evolving Patterns in Inpatient Pediatric Consultations to Allergy/Immunology at an Academic Medical Center

Madeline Wurst,[1] Anna Brameli,[2] Matthew Krantz,[2] R. Stokes Peebles, Jr.[2] Yasmin Khan,[3] Cosby A. Stone, Jr.[4]

Abstract

Background: Consultations to pediatric allergy/immunology are of benefit to many hospitalized inpatients, but there is limited current information about how T-cell receptor excision circles (TREC) screening may have changed these patterns for pediatric populations. We aimed to determine the types of consults being requested and their relative frequencies for primary pediatric allergy/immunology consults under an academic fellowship program since the start of TREC screening in 2016. Information gained could help identify focal concepts for pediatric allergy inpatient training curricula for fellowship and graduate medical education programs. **Methods**: Under an IRB approved study of an academic allergy fellowship consultation log, we retrospectively reviewed electronic medical records of pediatric allergy and immunology consults and categorized consultations by their primary indication. **Results**: Three-hundred and eighty-three pediatric allergy/immunology consultations were seen between September 4, 2016 to November 24, 2022. In terms of frequency, the most common consultation was for immunodeficiency evaluation or treatment, n=205 (53.5%), followed by drug allergy n=55 (14.4%), general allergy concerns n=43 (11.2%), skin allergy n=35 (9.1%), and less commonly inflammatory syndromes, n=26 (6.8%) and food allergy, n=19 (5.0%). Questions related to TREC screening comprised 21% of all immunodeficiency consults, at n=43. **Conclusion**: At an academic allergy center where all allergy/immunology service lines are currently provided, the most common reason for pediatric consultations were for help with immunodeficiency evaluation/treatment and drug allergy. TREC screening is a new key indication for consultation. Fellowship programs may benefit from focusing on these content areas for the pediatric inpatient setting.

Introduction

Allergy and Immunology are increasingly important disciplines as the rates of pediatric and adult allergies continue to rise and treatments for immunodeficiency improve. According to the CDC in 2021, over 1 in 4 children in the United States report having seasonal, food, or skin allergy.[1] Allergist/Immunologists within both the pediatric and adult patient population care for a wide variety of isolated or systemic disorders, ranging from autoimmune, inflammatory, and allergic conditions to diseases relating to immunodeficiency. Within the field of pediatric allergy/immunology, some commonly followed conditions include allergic rhinitis, allergic conjunctivitis, drug allergy, food allergy, anaphylaxis, atopic dermatitis, urticaria, angioedema, asthma, common variable immunodeficiency, congenital immunodeficiencies, etc. Training clinically and in the field of research allows of these clinicians to see and treat a wide variety of allergic and immunologic disorders both in the inpatient and outpatient setting.

Consultations to Pediatric Allergy/Immunology are of benefit to many hospitalized inpatients, but there is limited information about the scenarios under which allergists are currently consulted in pediatric inpatient care. Such information might help Allergy/Immunology fellowship training programs and graduate medical education programs develop their Pediatric Allergy/Immunology curricula. Therefore, we sought to retrospectively determine the types and frequencies of Pediatric Allergy/Immunology consults being requested from an academic fellowship program within the Vanderbilt Monroe Carell Children's Hospital System.

Severe combined immunodeficiency disorder (SCID) refers to many disorders that culminate in a deficient functional T cell phenotype and represents the most severe form of immunodeficiency in the pediatric patient population. Previously, clinical suspicion to further explore and identify SCID was based off recurrent and often fatal infectious complications. T-cell receptor excision circles (TRECs) are stable circular DNA molecules generated during the development of T cell receptor diversification in the thymus. By recombining genes in the anticipation of any foreign antigen presented to the body, TRECs are a subsequent byproduct formed and can serve as an indicator for recently produced naïve T cells. Integrating TREC measurement as a part of newborn screening (NBS) guidelines has allowed for the initiation of life-saving treatment and reinstatement of a functional immune system in an infant otherwise susceptible to life-threatening infection.[2,3]

[1] Third-year Medical Student. University of Tennessee Health Science Center College of Medicine, Memphis, TN, USA.

[2] MD. Division of Allergy, Pulmonary and Critical Care Medicine, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA.

[3] MD. Division of Allergy, Immunology, and Pulmonary Medicine, Department of Pediatrics, Vanderbilt University Medical Center/Monroe Carell Children's Hospital, Nashville, TN, USA.

[4] MD, MPH. Division of Allergy, Pulmonary and Critical Care Medicine, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA.

About the Author: *Madeline Wurst is currently a third-year medical student at the University of Tennessee Health Science Center in Memphis, Tennessee, a four-year program.*

Correspondence:

Madeline Wurst

Address: 62 S. Dunlap Street, Ste 300. Memphis, TN 38163-0001. Country. United States.

Email: mwurst@uthsc.edu

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Importantly, we sought to investigate the current information about how new practices of TREC screening in newborns may have changed patterns in Allergy/Immunology consultation for pediatric populations.

Methods

Design and Study Population

This was a cross-sectional descriptive study. The patient population consisted of 383 pediatric allergy/immunology patients whose records of consultation were collected retrospectively in a HIPAA compliant REDCap[4] consultation log between September 4, 2016 to November 24, 2022. This time period allowed for the capture of a comprehensive dataset pertinent to the introduction of TREC as part of newborn screening in the state of Tennessee starting January 2016. Inclusion criteria included pediatric patients consulted to allergy/immunology within this time frame with an age range from 0 days up to, but not exceeding, 18 years of age. Exclusion criteria included patients greater than the age of 18 years and consultations falling outside the study's defined time frame. Convenience sampling was employed to include all relevant consultations within the specified time frame and accurately assess their relative frequencies. A retrospective review approach was employed to collect consultation records under an IRB approved study (#211354), to review the log and electronic medical records from these pediatric allergy and immunology consults, and subsequently categorize these consultations by their primary indication.

Statistical Methodology

Categorization of primary reason for consult was based on broadly observed categories of immunodeficiency evaluation, inflammatory syndromes, drug allergy, food allergy, skin allergy, and general allergy (which included asthma, idiopathic anaphylaxis, urticaria/angioedema, rhinitis). Each primary reason was then subcategorized to create a deeper understanding of the reason for consultation and identify any large groupings. In cases where patients had multiple reasons for consultation, only the primary reason for consultation counted toward the patient's finalized categorization and subcategorization. For instance, a patient could be consulted for severe eczema and amoxicillin allergy. Through further chart review, it could be discovered the primary focus of the consultation was for severe eczema. Drug allergy may have remained part of the clinical question for consultation; however, after further investigation it was not clinically relevant to their current need for impatient consultation service nor had impact on their current hospital stay. Such complex cases often required chart review to discover true etiology of consultation need and help clarify proper and primary category and subcategory placement.

Categorical statistical calculation was employed by comparing the number of patients assigned to each category to the overall study population (n=383). Subcategorical statistical calculation was employed by comparing the number of patients assigned to each subcategory to the number of patients assigned to the broader category (e.g., FPIES n=6 (31.6%) where food allergy n=19). Percentages of respective categorical and subcategorical groupings were utilized for gross comparison of frequency of consultation.

Results

Patient Characteristic and Categorization Results

The age distribution of the cohort of Pediatric Allergy/ Immunology consults at Vanderbilt ranged from 0 days to 18 years (Mean, 6.06 years, SD = 6.71 years). The gender distribution included n=203 (53.3%) males and n=178 (46.7%) females. During years for which we had complete calendar data (2017-2021), we observed 47 consultations performed in 2017, 79 in 2018, 58 in 2019, 55 in 2020, and 74 in 2021 (***Table 1***). In terms of frequency, the most common consultation was for immunodeficiency evaluation or treatment, n=205 (53.5%), followed by drug allergy n=55 (14.4%), general allergy concerns n=43 (11.2%), skin allergy n=35 (9.1%), and less commonly inflammatory syndromes, n=26 (6.8%) and food allergy, n=19 (5.0%). Questions related to TREC screening comprised 11% of all consults, at n=43 (21% of all immunodeficiency consults) as shown in ***Table 2***.

Table 1. **Patient Characteristics of 383 Pediatric Allergy and Immunology Consultations During the Study Period.**

Patient Characteristic	Frequency (n)	%
Age at Time of Consultation **(n = 379)	6.06 years (±6.71)*	
Reported Sex (n = 381) **		
Males	203	53.3
Females	178	46.7
Year of Consultation (n=382)**		
Sep 4th '16-Dec 31st '16	16	4.2
2017	47	12.3
2018	79	20.7
2019	58	15.2
2020	55	14.4

Legend: *mean ± SD. ** small numbers of patients with missing age, sex, and year of consultation data.

Patient Subcategorization Results

One hundred and four (51%) of 205 consultations for immunodeficiency were either requests to evaluate immune function or related to TREC screening results. Additional immune evaluation subcategories included secondary immunodeficiency in undiagnosed patients, such as lymphopenia, hypoplastic left heart syndrome (HLHS), etc. Other reasons for pediatric immunodeficiency consult included frequent, recurrent or disseminated infections, n=35 (17.1%), IVIG management, n=32 (15.6%), congenital syndromes, n=22 (10.7%), fever, n=7 (3.4%), management of diagnosed immunodeficiency, n=3 (1.5%), and immunodeficiency associated with transplant, n=2 (1.0%), as shown in ***Table 2***.

Table 2. **Patient Categories and Subcategories of 383 Pediatric Allergy and Immunology Consultations During the Study Period.**

Consults Received	Category Consultation (n)	Overall Consultation (%)
Immune Evaluation	*205*	*53.5*
TREC screening	43	21.0
Infection	35	17.1
IVIG management	32	15.6
Congenital Syndrome	22	10.7
Fever	7	3.4
Diagnosed Immunodeficiency	3	1.5
Transplant	2	1.0
Drug Allergy	*55*	*14.4*
Antimicrobial	32	58.2
Other Drug	11	20.0
DRESS/SJS	6	10.9
Contrast Media	4	7.3
Reaction During Catheterization	2	3.6
General Allergy	*43*	*11.2*
Angioedema (± anaphylaxis)	20	46.5
Anaphylaxis only	18	41.9
Asthma (± anaphylaxis)	3	7.0
Nasal Secretions	1	2.3
Vocal Cord Dysfunction	1	2.3
Skin Allergy (n = 35)	*35*	*9.1*
Urticaria (± angioedema)	15	42.9
Eczema	13	37.1
Rash	3	8.6
Contact Dermatitis	2	5.7
Erythema	1	2.9
Skin Care	1	2.9
Inflammatory Syndromes (n = 26)	*26*	*6.8*
IBD/Colitis	10	38.5
Mastocytosis/Hypereosinophilia/ Hyper IgE	9	34.6
Recurrent Fever	3	11.5
HLH	2	7.7
Cytokine Storm	1	3.9
Food Allergy	*19*	*5.0*

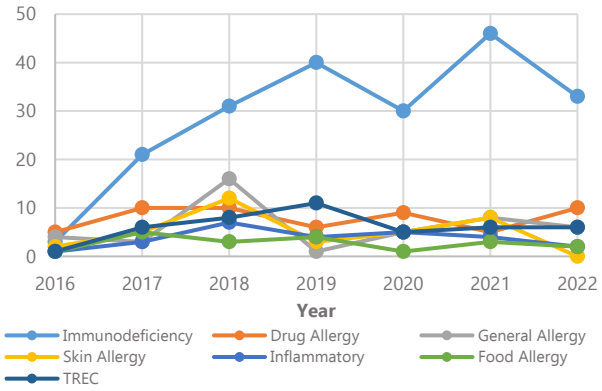
Legend: *mean ± Standard deviation. ** small numbers of patients with missing age, sex, and year of consultation data. Immunodeficiency subcategories include infections requiring workup, IVIG therapy management, congenital syndromes, fever indicating immunodeficiency, prior diagnoses needing care, and transplant-related complications. Drug allergy subcategories cover non-antimicrobial allergies and severe reactions (DRESS/SJS). General allergy includes angioedema and anaphylaxis consultations, while skin allergy covers urticaria and eczema cases.

Drug allergy comprised 14.4% of consultation requests, for which 58% of drugs were antimicrobials, consistent with their prominent therapeutic role.[5] Drug challenges were performed in 3 patients and desensitization for 1 patient, together comprising 12.5% of the antimicrobial subcategory. Reasons for pediatric drug allergy consults also included other drugs specified, n=11 (20.0%), Drug Rash with Eosinophilia and Systemic Symptoms and Stevens-Johnson syndrome (DRESS/SJS), n=6 (10.9%), contrast media reaction, n=4 (7.3%), and reaction during a catheterization, n=2 (3.6%), as shown in ***Table 2***.

Angioedema and idiopathic anaphylaxis comprised 88% of the primary reasons for general allergy consults. Other general allergy subcategories included asthma, n=3 (7.0%), nasal secretions/rhinitis, n=1 (2.3%), and vocal cord dysfunction, n=1 (2.3%) as shown in ***Table 2***.

Urticaria and eczema/atopic dermatitis comprised 80% of the primary reasons for skin allergy consult. Other subcategories for skin allergy consult included rash, n=3 (8.6%), contact dermatitis, n=2 (5.7%), erythema, n=1 (2.9%), and questions about how to perform skin care, n=1 (2.9%) as shown in ***Table 2***.

Figure 1. **Number of Category and T-cell receptor excision circles (TREC) Consults per Year.**



Legend: The Mann-Kendall test was used to determine Kendall's tau correlations for the number of consults in each category from 2017-2021, excluding 2016 and 2022 due to incomplete data. For immunodeficiency, the correlation was 0.600 (p = 0.142); for drug allergy, -0.738 (p = 0.077); for general allergy, 0.200 (p = 0.624); for skin allergy, 0.200 (p = 0.624); for inflammatory, 0.316 (p = 0.448); for food allergy, -0.527 (p = 0.207); and for TREC, -0.105 (p = 0.801).

Inflammatory syndromes and food allergy together comprised 12% of the overall consultations, comprising the least common reason for Allergy/Immunology consults. Inflammatory bowel disease/colitis, n=10 (38.5%), and mastocytosis/ hypereosinophilia/hyper IgE syndromes, n=9 (34.6%), comprised the largest subcategories for inflammatory syndrome consult. Other subcategories for inflammatory syndrome consult included recurrent fever, n=3 (11.5%), hemophagocytic lymphohistiocytosis (HLH), n=2 (7.7%), cytokine storm, n=1 (3.8%), and hypersensitivity pneumonitis, n=1 (3.8%). General food allergy, n=11 (57.9%), comprised the largest subcategory of food allergy, with other subcategories including food protein-induced enterocolitis syndrome (FPIES), n=6 (31.6%), and alpha-gal syndrome, n=2 (10.5%) as shown in ***Table 2***.

Mann-Kendall test was utilized to identify Kendall's tau correlation between number of consults in each category as well as TREC subcategorization over time, including only years 2017-2021 due to incomplete yearly data from 2016 and 2022. Overall, there was not a significant trend of change of category or TREC consultations over the study period as shown in **Figure 1**.

Discussion

Key Findings

Overall, the highest area for consultation was immunodeficiency, followed by drug allergy, general allergy, skin allergy, inflammatory syndromes, and food allergy. Of interest, the highest subcategorization of immunodeficiency consultations was to evaluate immune function and second highest relating to TREC screening results. There was no significant trend in category or TREC consultation change over time, which may be seen due to limited amount of consultations made to inpatient pediatric allergy/immunology as a field to the inpatient setting. A multicenter study with larger study population may be employed in the future to rectify a potential type 2 error. Within this greater context, immunodeficiency is clearly a key, prominent area for inpatient pediatric consultation at our center, followed by drug allergy consultations. Conversely, at our medical center, anaphylaxis, food allergy, and asthma exacerbations requiring hospitalization are typically managed by the inpatient general pediatric team with outpatient follow up in allergy/immunology, without the need for allergy consultation, which may differ at other institutions.

Investigation of Relevant Literature

The results of this study are interesting when contrasted with a few earlier studies that are available. In contrast to a previous study reviewing pediatric inpatient consults to Allergy/Immunology from 1995 to 1999, where immunodeficiency evaluations accounted for only 9.7% of cases, our dataset revealed a notably increased shift, comprising 53.5% of our dataset. This stark difference underscores the evolving landscape of pediatric healthcare, with asthma remaining the primary consultation category at 58% in the earlier study.[6] This earlier study also found that ruling out DiGeorge syndrome was the leading reason for immunodeficiency evaluation.[6] In contrast, congenital syndromes accounted for only 11% of reason for immunodeficiency consults in our patient population. Compared to a study by Kim et al. from 1999-2013, we found that asthma was not our predominant reason for pediatric consultation, but the order of common indications was similar thereafter.[7] Our findings are similar to those of Kempe et al, who reported on consultations at a pediatric academic center with immunodeficiency services between 2009-2014. However, the addition of newborn TRECs screen has added a new high-volume indication for consults.[8] Compared to studies from other centers, the frequency of consultations for food allergy, inflammatory syndromes and skin allergy in this study are similar, suggesting that allergy/immunology is not the primary service involved in acute management of most of these events. Future research may be necessary to elucidate the reasoning behind the overall increase in immunodeficiency consultations compared to studies from previous time periods.

Impact of TREC in Newborn Screening

Tennessee initiated TREC screening in newborns in the year 2016, which likely corresponds with the high rates of TREC consults reasons seen within the timeframe of this study.[9] SCID is considered a pediatric emergency with a high mortality within the first 1 to 2 years of life if left untreated. Bone marrow transplant of patients <3.5 months of age and without infection has been shown to improve their overall survival.[10] Furthermore, patients diagnosed earlier through NBS were less likely to develop infection before bone marrow transplantation.[11] Similar success has been found in long-term outcome follow-up.[12] Our study demonstrates real change in the wake of TREC becoming part of newborn screening in 2016, with a high volume of relevant consultations.

Impact of Physician Education

It has been shown that implementing educational opportunities increases physician knowledge of immunodeficiency.[13] This can thereby increase early detection and subsequently initiate lifesaving treatment in a time sensitive manner for relevant populations. This is especially relevant in the wake of increasing immunodeficiency related consultations as seen in this study. Most allergy/immunology programs are relatively small and therefore place a significant burden on program faculty to prepare content for learners in areas they may only rarely encounter themselves. Therefore, educational gaps may be in place when trying to teach the next generation of physicians the knowledge base that is necessary for continuity of this field.[14] Alongside the increase of telemedicine utilization in medical practice there is an additional increase in online educational opportunities and support for physicians practicing in the field of immunodeficiency. Medical education programs and listserves utilizing these growing resources and closing these educational gaps remains imperative to further proper patient care while there continue to be rapid gains of knowledge and evolution in the allergy/immunology field.

Limitations

Our study may have limitations in generalizability due to being conducted at a single, academic, tertiary medical center. However, the breadth of consulting services and relevant expertise in different aspects of allergy/immunology at a tertiary center may also identify the range of consults it is possible to receive. Limitations of this study may also include inability to rule out occasional missing data on consultations performed during this time period.

Conclusion

In conclusion, at an academic allergy center where all pediatric Allergy/Immunology service lines are currently provided, the most common reasons for pediatric consultation were for immunodeficiency evaluation/treatment and drug allergy, suggesting that these two areas may have a higher rate of needs specific to the inpatient setting. With recent rapid changes occurring in both of these content areas, fellowship programs may benefit from a training focus in immunology, pediatric immunodeficiency, and drug allergy relevant to the pediatric inpatient setting. Our findings suggest that formal training on the implications and evaluation of TREC screening results and common drug allergy scenarios should be a part of the core pediatric allergy/immunology curriculum at every fellowship. In particular, the inclusion of TREC testing in neonatal screens has resulted in a prominent subcategory of consultations that will likely need a specific focus when educating future clinicians.

Summary – Accelerating Translation

Understanding the Patterns of in Pediatric Inpatient Allergy and Immunology Consultations

Main Problem to Solve: Pediatric allergies and immunological issues continue to be on the rise and even require intervention in the hospital; however, there is still limited information out there as to the key reasons for consulting such specialists. This study aimed to investigate reasons behind consultation to Allergy/Immunology services in the inpatient setting as new technology and screening practices continue to evolve. In 2016, TREC was introduced as part of the newborn screen, which checks for serious and rare treatable health conditions at birth. This implementation was especially important for the early diagnosis and treatment of severe combined immunodeficiency disease (SCID), a group of rare and life-threatening diseases that can severely impact the ability of a child to fight infection. As such, we sought to investigate the current information about how new practices of TREC screening in newborns may have changed these patterns of consultation for pediatric populations.

Aim of the Study: The goal of this study was to uncover the types and frequencies of pediatric allergy and immunology consultations within the Vanderbilt Monroe Carrel Children's Hospital System. Identifying patterns in consultations and assessing how new practices, such as the introduction of TREC as part of Newborn Screening, would influence key reasons for seeking specialized care. This could provide valuable information for medical training programs to help tailor their curricula to meet the evolving needs of patients and physicians.

Methodology: This study included 383 hospitalized pediatric patients who sought allergy/immunology consultations between September 2016 and November 2022. All records collected ensured the legal right to medical privacy was maintained. Following review of the consultation logs and electronic medical records, consultations were categorized based on primary reasons for allergy/immunology subspecialty involvement. Top primary reasons for consult included of immunodeficiency evaluation, inflammatory syndromes, drug allergy, food allergy, skin allergy, and general allergy. These reasons were then further subdivided to gain a deeper understanding of the specific issues prompting consultation.

Results: The age range of pediatric patients seeking allergy/immunology consultations in the hospitalized setting at Vanderbilt ranged from 0 days to 18 years. The gender distribution was relatively balanced, with slightly more males (53.3%) than females (46.7%). In terms of frequency, the most common primary reasons for consultation included immunodeficiency evaluation or treatment (53.5%), followed by drug allergy (14.4%), general allergy (11.2%), skin allergy (9.1%), inflammatory syndromes (6.8%), and less commonly food allergy (5.0%).

The study identified specific subcategories within each primary reason to offer a more detailed look into consultation reasoning. Importantly, from this it was found that questions related to TREC screening comprised 21% of all immunodeficiency consults and 11% of all total consults.

Conclusion: The results of this study show the diverse reasons for Allergist and Immunologist need within the pediatric inpatient setting. Immunodeficiency and drug allergy related consultations emerged as the most common reasons for seeking specialized care. Notably, the inclusion of TREC screening as part of Newborn Screening practices across the nation starting in 2016 has impacted consultation patterns as compared to earlier scientific studies on this topic. This shows how dynamic the field of pediatric allergy and immunology care are as medical and technological advances continue to progress. This is especially important in the cases of life-threatening disease where early intervention is imperative towards child survival, such as in SCID.
In conclusion, this study suggests that for allergy and immunology experts, there is a higher rate of need for immunodeficiency evaluation/treatment and drug allergy intervention in the inpatient setting. The findings underscore the importance of adapting education to address evolving trends and incorporating new screening practices into training programs. In particular, the inclusion of TREC testing in neonatal screens has resulted in a prominent subcategory of consultations that will likely need a specific focus when educating future clinicians. By doing so, medical professionals can stay well-equipped to handle the changing landscape of pediatric allergy and immunology and ensure optimal care.

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