Dermatology Update 2017
Pediatric Dermatology

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Updates

July 2016 - July 2017

- Atopic dermatitis
- Vascular malformations
- Anesthesia
- Allergies
- Teenagers…

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NEW THERAPIES

New Therapies!

- Crisaborole 2% ointment
- Dupiliumab
  - IL4 receptor antagonist
  - Approved for adults (≥18yo) with moderate-severe atopic dermatitis
    - Blauvelt et al. *Lancet* 2017; 389(10086)
  - Pediatric studies still pending

Crisaborole 2% Ointment

- PDE4 inhibitor → decrease inflammation
- FDA approved for mild-moderate atopic dermatitis ≥2 years old
- Twice daily application
- SE: burning, stinging

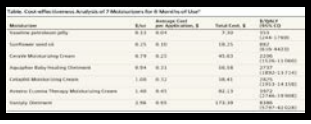
Paller et al. *JAAD* 2016;75(3)
Zane et al. *Am J Clin Dermatol* 2016;17

PREVENTION

JAMA Pediatrics | Original Investigation

Cost-effectiveness of Prophylactic Moisturization for Atopic Dermatitis

- Daily moisturization of high risk neonates/infants for 6-8 months decreases the incidence of AD
  - High risk = 1st degree relative with AD, asthma, allergic rhinitis
  - Sunflower seed oil, Aquaphor, Cetaphil cream
  - Improved skin barrier



Horimukai et al. *J Allergy Clin Immunol* 2014;134(4)
Simpson et al. *J Allergy Clin Immunol* 2014;134(4)
Xu et al. *JAMA Pediatrics* 2017;171(2)

Early Probiotic Supplementation for Eczema and Asthma Prevention: A Randomized Controlled Trial

- Does *Lactobacillus rhamnosus* administration from 0-6mo decrease eczema and asthma?
  - 1 parent had asthma
  - 184 infants
  - 10 billion CFU LGG and 225mg inulin vs inulin
  - Endpoints: eczema or asthma w/in 2 years
  - Conclusion: no significant decrease in hazard ratio

Kalliomäki et al. *Lancet* 2001; 357(9262)
Kopp et al. *Pediatrics!* 2008;121(4)
Cabana et al. *Pediatrics* 2017;140(3)

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HEMANGIOMAS

Predisposing Factors

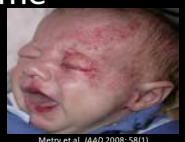
- Multiple gestation
- Female
- IVF
- CVS, amniocentesis
- Placental abnormalities
- Low birth weight
- Prematurity
- **Gestational hypertension, pre-eclampsia**
- **Maternal progesterone use**
- **Gestational diabetes**

Prenatal Risk Factors for Infantile Hemangioma Development

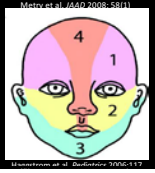
PHACE SYNDROME

PHACE Syndrome

- **P**osterior fossa malformation
- **H**emangioma
- **A**rterial anomalies
- **C**oarctation of the aorta/**c**ardiac defects
- **E**ye abnormalities
- **S**ternal clefting/**s**upraumbilical abdominal raphe



Metry et al. JAAD 2008; 58(1)

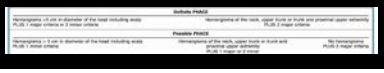


PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations

J Pediatr 2016 178:24

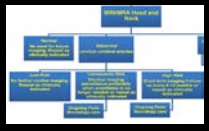
PHACE Update

- Screen:
  - Segmental hemangioma of the head (face or scalp), >5cm
  - Segmental hemangioma of the neck, upper trunk, trunk and proximal upper extremity PLUS major finding in PHACE
  - No hemangioma but other findings in PHACE
- PHACE if:



PHACE Update

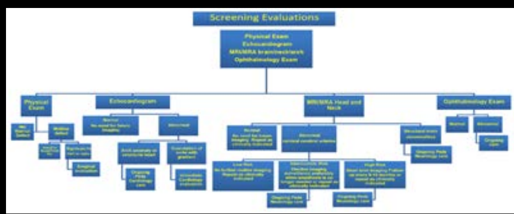
- Arteriopathy and the risk of strokes
  - Findings risk stratified



PHACE Update

- Long term morbidity
  - Caution using propranolol in severe arteriopathy
  - Headaches
  - Speech and language delays
  - Thyroid dysfunction, hypopituitarism
  - Dental enamel hypoplasia

PHACE Evaluation



Garzon et al. *J Pediatr* 2016 178:24

Propranolol and Development

Propranolol treatment of infantile hemangioma (IH) is not associated with developmental risk or growth impairment at age 4 years

Andre Vadimovich Moyakine, MD,* Jorien Maria Kerstjens, MD, PhD,* Saskia Spillekom-van Koulil, MSc, PhD,* and Catharina Joanna Maria van der Vleuten, MD, PhD*
Nijmegen and Groningen, The Netherlands

JAAD 2016; 75!1)

Pediatric Dermatology 1–5, 2017

Study of Cognitive Function in Children Treated with Propranolol for Infantile Hemangioma

Nieves González-Llorente,* Isabel del Olmo-Benito,* Natalia Muñoz-Ollero,* Miguel Angel Descalzo, M.D.,† Ignacio García-Doval, M.D.,† and Antonio Torrelo, M.D.‡

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Propranolol treatment of infantile hemangioma (IH) is not associated with developmental risk or growth impairment at age 4 years

JAAD 2016; 75!1)

- 82 children treated with propranolol
  - Started 4.8mo
  - 2-3mg/kg/day
  - Treated 12.9 months
  - Age control matched
- At 4 years

Table III. Number of children with abnormal 48-months Ages and Stages Questionnaire scores

Abnormal ASQ*	Propranolol-treated IH, n = 82	Control group, n = 82	P value†
Fine motor	1 (1.2%)	4 (4.9%)	.17
Gross motor	2 (2.4%)	4 (4.9%)	.41
Communication	1 (1.2%)	1 (1.2%)	1.00
Problem solving	1 (1.2%)	1 (1.2%)	1.00
Personal-social functioning	2 (2.4%)	2 (2.4%)	1.00

ASQ, Ages and Stages Questionnaire; *IH*, infantile hemangioma.
*Abnormal score for ≥1 domain.
†Based on χ^2 test.

Pediatric Dermatology 1–5, 2017

Study of Cognitive Function in Children Treated with Propranolol for Infantile Hemangioma

- 23 5-7yo treated with propranolol as infants
- 2mg/kg/d for 7.5 months on average
- Cognitive function and memory testing
- Result:

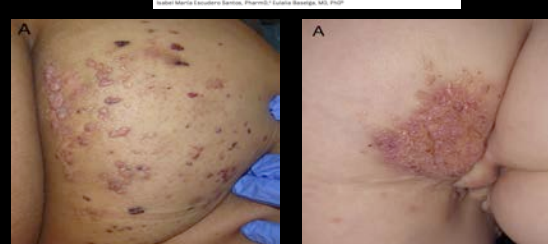
TABLE 2. *Comparison Study Population Data in Relation to the Normal Distribution (Shapiro–Wilk Test) (N = 23)*

Variable	Mean	95% confidence interval	Standard deviation	p-Value
Spanish Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition				
Comprehension	[illegible]	[illegible]	[illegible]	0.12
Intelligence	[illegible]	[illegible]	[illegible]	0.01*
Test of Memory and Learning				
Verbal memory index	[illegible]	[illegible]	[illegible]	[illegible]
Nonverbal memory index	[illegible]	[illegible]	[illegible]	[illegible]
Composite memory index	[illegible]	[illegible]	[illegible]	[illegible]
Delayed recall index	[illegible]	[illegible]	[illegible]	[illegible]

*This p-value is significant for an abnormally high composite score of intelligence in one patient.

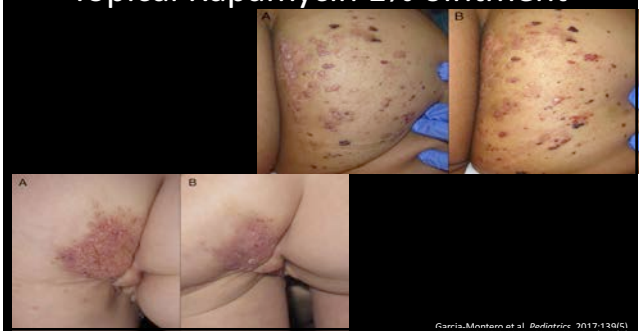
LYMPHATIC MALFORMATIONS

Microcystic Lymphatic Malformation Successfully Treated With Topical Rapamycin



Garcia-Montero et al. *Pediatrics* 2017;139(5)

Topical Rapamycin 1% ointment



Garcia-Montero et al. *Pediatrics*. 2017;139(5)

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THE RISK OF ANESTHESIA

[4-27-2017] The U.S. Food and Drug Administration (FDA) is notifying the public that we have approved previously announced label changes regarding the use of general anesthetic and sedation medicines in children younger than 3 years. These changes include:

- A new Warning stating that exposure to these medicines for lengthy periods of time or over multiple surgeries or procedures may negatively affect brain development in children younger than 3 years.
- Addition of information to the sections of the labels about pregnancy and pediatric use to describe studies in young animals and pregnant animals that showed exposure to general anesthetic and sedation drugs for more than 3 hours can cause widespread loss of nerve cells in the developing brain; and studies in young animals suggested these changes resulted in long-term negative effects on the animals' behavior or learning.

General anesthetic and sedation drugs are necessary for patients, including young children and pregnant women, who require surgery or other painful and stressful procedures. In the U.S., surgeries during the third trimester of pregnancy requiring general anesthesia are performed only when medically necessary and rarely last longer than 3 hours. We are advising that in these situations, pregnant women should not delay or avoid surgeries or procedures during pregnancy, as doing so can negatively affect themselves and their infants.

Similarly, surgeries or procedures in children younger than 3 years should not be delayed or avoided when medically necessary. Consideration should be given to delaying potentially elective surgery in young children where medically appropriate.

Association Between a Single General Anesthesia Exposure Before Age 36 Months and Neurocognitive Outcomes in Later Childhood

Lena S. Sun, MD, Guohua Li, MD, DrPH, Tonya L. K. Miller, MD, Cynthia Salorio, PhD, Mary W. Byrne, PhD, MPH, David C. Bellinger, PhD, MSc, Caleb Ing, MD, MS, Raymond Park, MD, Jerilynn Radcliffe, PhD, Stephen R. Hays, MD, MS, Charles J. DiMaggio, PhD, Timothy J. Cooper, PsyD, Virginia Rauh, ScD, Lynne G. Maxwell, MD, Ahrim Youn, PhD, and Francis X. McGowan, MD

JAMA 2016;315(21)

Neurodevelopmental outcome at two years of age after general and awake-regional anaesthesia in infancy: a randomised controlled trial

Andrew J. Davidson, MD,[1,2,3] Nicola Disma, MD,[4] Jurgen C. de Graaff, PhD,[5] Davinia E. Withington, BM,[6,7] Liam Dorris, DClinPsy,[8,9] Graham Bell, MBChB,[10] Robyn Stargatt, PhD,[11,12] David C. Bellinger, PhD,[13,14,15] Tibor Schuster, PhD,[16] Sarah J. Arnup, MBiostat,[16] Pollyanna Hardy, MSc,[17] Rodney W. Hunt, PhD,[3,18,19] Michael J. Takagi, PhD,[1,12] Gaia Giribaldi, MD,[4] Penelope L. Hartmann, BPsych(Hons),[1] Ida Salvo, MD,[20] Neil S. Morton, MD,[10,21] Britta S von Ungern-Sternberg, PhD,[22,23] Bruno Guido Locatelli, MD,[24] Niall Wilton, MBBS,[25] Anne Lynn, MD,[26] Jose J. Thomas, MD,[27] David Polaner, MD,[28] Oliver Bagshaw, FRCA,[29] Peter Szmuk, MD,[30] Anthony R. Absalom, MBChB,[31] Geoff Frawley, MBBS,[1,2] Charles Berde, MD,[32] Gillian D Ormond, MSc,[1] Jacki Marmor, MEd,[13] Mary Ellen, McCann,[32] and The GAS Consortium

Lancet 2016;387(10015)

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JAMA 2016;315(21)

- Sibling matched cohort study when one sibling had inguinal hernia repair at <36mo assessed at 8-15 years of age.
- Assessed global cognitive functioning and domain specific neurocognitive functions and behavior.
- No statistically significant differences in mean scores were found between sibling pairs in memory/learning, motor/processing speed, visuospatial function, attention, executive function, language, or behavior

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Lancet 2016;387(10015)

- Infants <60 weeks postmenstrual age and >26 weeks gestation with inguinal hernia repair
- Randomized to regional or general anesthesia
- Interim result at 2 years old – cognitive, motor, and language assessment
- No statistically significant difference between groups

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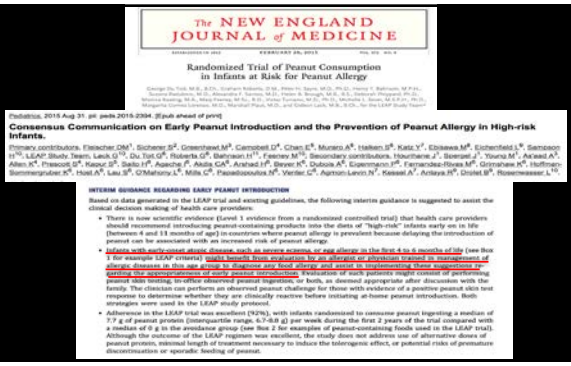
PEANUT ALLERGY PREVENTION



The NEW ENGLAND JOURNAL of MEDICINE

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

Pediatrics. 2015 Aug 31. pii: peds.2015-2394. [Epub ahead of print]

Consensus Communication on Early Peanut Introduction and the Prevention of Peanut Allergy in High-risk Infants.

INTERIM GUIDANCE REGARDING EARLY PEANUT INTRODUCTION

Based on data generated in the LEAP trial and existing guidelines, the following interim guidance is suggested to assist the clinical decision making of health care providers:

- There is now scientific evidence (Level 1 evidence from a randomized controlled trial) that health care providers should recommend introducing peanut-containing products into the diets of "high-risk" infants early on in life (between 4 and 11 months of age) in countries where peanut allergy is prevalent because delaying the introduction of peanut can be associated with an increased risk of peanut allergy.
- Infants with early-onset atopic disease, such as severe eczema or egg allergy in the first 4 to 6 months of life (see Box 1 for example LEAP criteria) might benefit from evaluation by an allergist or physician trained in management of allergic diseases in this age group to diagnose any food allergy and assist in implementing these suggestions regarding the appropriateness of early peanut introduction. Evaluation of such patients might consist of performing peanut skin testing, in-office observed peanut ingestion, or both, as deemed appropriate after discussion with the family. The clinician can perform an observed peanut challenge for those with evidence of a positive peanut skin test response to determine whether they are clinically reactive before initiating at-home peanut introduction. Both strategies were used in the LEAP study protocol.
- Adherence in the LEAP trial was excellent (92%), with infants randomized to consume peanut ingesting a median of 7.7 g of peanut protein (interquartile range, 6.7–8.8 g) per week during the first 2 years of the trial compared with a median of 0 g in the avoidance group (see Box 2 for examples of peanut-containing foods used in the LEAP trial). Although the outcome of the LEAP regimen was excellent, the study does not address use of alternative doses of peanut protein, minimal length of treatment necessary to induce the tolerogenic effect, or potential risks of premature discontinuation or sporadic feeding of peanut.

Togias A, Cooper SF, Acebal ML, et al. Addendum guidelines for the prevention of peanut allergy in the United States: report of the NIAID- sponsored expert panel. *J Allergy Clin Immunol*. 2017;139(1):29–44

TABLE 1 Summary of Addendum Guidelines

Infant Criteria	Recommendations	Earliest Age of Peanut Introduction
Guideline 1. Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE or SPT and, if necessary, an oral food challenge. Based on test results, introduce peanut-containing foods.	4–6 mo
Guideline 2. Mild to moderate eczema	Introduce peanut-containing foods.	Around 6 mo
Guideline 3. No eczema or any food allergy	Introduce peanut-containing foods.	Age appropriate and in accordance with family preferences and cultural practices

Sicherer et al. *Pediatrics* 2017;138(6)

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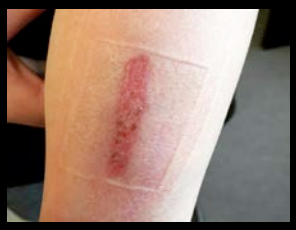
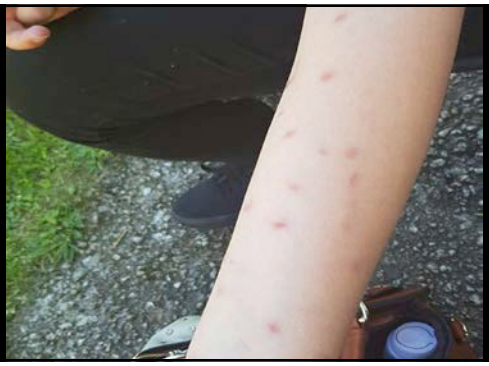
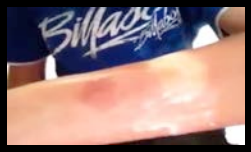
Salt Ice Challenge



Eraser Challenge





Deodorant Challenge

- Aerosol deodorant sprayed onto the skin for as long as possible or as many times as possible

Updates

July 2016 - July 2017

- Atopic dermatitis
  - Crisaborole!
  - Daily moisturization is cost effective to decrease AD in high risk infants, but *lactobacillus* supplementation isn't effective
- Vascular malformations
  - Gestational diabetes is a risk factor for hemangiomas
  - PHACE diagnosis: Garzon et al. *J Pediatr* 2016 178:24
  - Does propranolol effect cognitive impairment? Maybe not
  - Topical rapamycin to treat microcystic lymphatic malformations
- Anesthesia
  - Preliminary studies indicate no significant difference in neurodevelopment between GA and non-GA exposed infants
  - FDA warning: exposure to GA/sedation for >3 hours or over multiple procedures may negatively impact brain development in children <3 years.
- Allergies
  - New published guidelines for how to introduce peanuts to infants
- Teenagers…
  - They do crazy things

Thank You