Translating Best Evidence into Best Care

EDITOR'S NOTE: Studies for this issue were identified using the Clinical Queries feature of PubMed, "hand" searching *JAMA Pediatrics, Pediatrics,* and *The Journal of Pediatrics*, and from customized EvidenceUpdates alerts.

EBM PEARL: STANDARDIZED INCIDENCE RATIO (SIR) AND EXCESS ABSOLUTE RISK: The SIR is the number of people with a particular disease in a specific population relative to what would be the number with that disease expected in a similar population (age, sex, calendar year, over a specific period of time). The expected number is calculated by multiplying the number of affected individuals in the general population per person-years of follow-up time, by the person-years of follow-up time in the cohort. In the study by Chiang et al (J Pediatr 2015;166:418-23), there were 20 patients with autistim disorder with cancer. The expected number, adjusted for the number of person years of follow-up was 10.31. The ratio of these two numbers, 20/10.31=1.94 is the SIR. The excess absolute risk is the difference of 20 and 10.31 divided by the person-years of follow-up time in the cohort: (20-10.31)/76,332 = 0.13 cancers/1000 person-years (see the piece by Blatt on page 208).

LITERATURE SEARCH PEARL: SLIDER INTERFACE FOR MEDLINE (SLIM): SLIM is quick way to search PubMed (http://www.ncbi.nlm.nih.gov/pubmed) by allowing for easy limit adjustment employing a slide-rule interface for each adjustment. The standard limits are represented, such as age, publication date, and citations to display. In addition, the methodologic quality filters have been included (the same ones as in the "clinical queries" section of PubMed), as well as one's choice of MeSH term application to the search. A "preview count" button gives quick feedback on how many citations were retrieved, without actually loading the citations until the "search" button is pressed. The SLIM search engine may be found at https://pmi.nlm.nih.gov/slim/ and is a quick approach to a methodologically high-level search with limits.

—Jordan Hupert, MD

Association of Autism with Cancer

Chiang HL, Liu CJ, Hu YW, Chen SC, Hu LY, Shen CC, et al. Risk of cancer in children, adolescents, and young adults with autistic disorder. *J Pediatr.* 2015;166:418-23.

Question Among children and adolescents, what is the association of autistic disorder (AD) with cancer?

Design Retrospective cohort study.

Setting Taiwan National Health Insurance Research Database, Registry for Catastrophic Illness Patients.

Participants Children and adolescents with AD enrolled in the databases from 1997 through 2011 at ages 1-20 years.

Intervention Analysis of database and registry.

Outcomes Number of cancers in patients with AD compared with the expected number.

Main Results Cancer occurred more frequently in patients with AD than the total number of expected cancers, with a standardized incidence ratio (SIR) estimate (number of AD patients with cancer divided by the expected number) of 1.94 (95% CI 1.18-2.99).

Conclusions Patients with AD have an increased risk of cancer.

Commentary This ambitious look at over 8000 children with AD benefited from sample size. However, anonymized database studies can be flawed by the quality of even stringently defined coding diagnoses. Validation of AD can be difficult, with both under- and overdiagnosis, leading to inaccuracies in calculating relative risks of comorbidities.[1] Cancer coding is suspect when pathology reports are not reviewed, even if they were the basis for database inclusion. Anatomic coding may have obscured associations with specific tumor types (eg, "ovarian cancers" could have been lymphomas or soft tissue sarcomas). Some histologically benign brain tumors may not have been identified, which may have contributed to the lack of association between these tumors and AD as has been suggested by a prior report.[2] Patients in whom a cancer diagnosis preceded that of AD were excluded and may have masked an association in young children. Even assuming that all AD and cancer designations were correct, the high SIR of a child with AD developing cancer did not convey a high excess absolute risk, which was only 0.13/1000 years of subject follow-up more than for population controls.[3] Results should be reassuring to families of children with AD, and should not trigger routine surveillance.

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Early peanut consumption is protective against peanut allergy development

Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015;372:803-13.

Question Among infants at high risk of peanut allergy, what is the therapeutic efficacy of early, compared with late peanut introduction, in the development of peanut allergy?

Design Stratified, randomized controlled trial.

Setting Single site in the United Kingdom.

Participants Infants, 4-10 months of age, at high risk for peanut allergy.

Intervention Consume or avoid peanuts until 60 months of age.

Outcomes Peanut allergy at 60 months of age.

Main Results Peanut allergy decreased among infants who consumed peanuts: number needed to treat, 9 (95% CI, 7 to 14) and 4 (95% CI, 3 to 12), for pre-study skin-prick negative and positive infants, respectively.

Conclusions Early introduction of peanuts significantly decreased allergy development.

Commentary This trial addresses an observation previously made by the authors,[1] that the rate of peanut allergy was 10-fold higher among Jewish children in the UK where peanut generally is avoided in the first year of life, compared with Israeli infants who ingest peanuts routinely. The compelling evidence in the current study supports the hypothesis that earlier introduction is protective. However, the translation of the findings into practice requires reflection. Participants were infants already having illnesses associated with developing peanut allergy, excluding those with stronger positive peanut allergy tests. Indeed, some infants reacted at the medically-supervised first exposure. Should physicians wish to recapitulate the study, attention must be paid to the following: (1) decisions regarding allergy skin testing; (2) supervising the first feeding; (3) instructions for dosing (the impact of different regimens are unknown); (4) addressing whether infants are "dependent" upon regimented peanut ingestion to remain tolerant; and (5) instructions about feeding, as peanuts and peanut butter are choking hazards. How the results apply to healthy infants is unknown. One could extrapolate that the study supports prior American Academy of Pediatrics[2] and American Academy of Allergy, Asthma and Immunology[3] conclusions that there is no evidence for avoiding any particular foods, including allergens such as peanut, to healthy infants at risk for allergy who are developmentally ready to ingest solids. Expert panels are working on recommendations based on this study.

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Prolonged postconcussive rest is not superior to usual care

Thomas DG, Apps JN, Hoffmann RG, McCrea M, Hammeke T. Benefits of strict rest after acute concussion: a randomized controlled trial. *Pediatrics* 2015;135:213-23.

Question Among children and adolescents with concussion, what is the therapeutic benefit of strict rest, compared with the currently recommended moderate stepwise rest approach, in significant post-concussive symptoms?

Design Randomized controlled trial. Unclear if outcome assessment was blinded.

Setting University of Wisconsin emergency department with follow-up at home or University.

Participants Children 11 – 22 years of age diagnosed with concussion, presenting to the emergency department within 24 hours of injury.

Intervention Strict rest for 5 days or usual care (stepwise return to activity after symptom resolution).

Outcomes Neurocognitive and balance assessments.

Main Results There were no clinically significant differences in neurocognitive or balance outcomes. However, the intervention group reported more daily postconcussive symptoms.

Conclusions Strict rest immediately after concussion offered no benefit over usual care.

Commentary The use of rest as a treatment tool in concussion remains the standard of care[1]; however, the most