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### USE OF ATYPICAL ANTIPSYCHOTICS IN PRIVATELY-INSURED MISSOURI YOUTH.

DR Halloran, J Swindle, SK Takemoto, Saint Louis University, St. Louis, MO.

**BACKGROUND:** Atypical antipsychotic medications (risperidone, olanzapine, clozapine, and quetiapine fumarate) have not been carefully studied in children despite a dramatic increase in their use. One study in a midwestern Medicaid population found a prevalence for atypical antipsychotics of 13 per 1000 children with psychiatric diagnoses such as attention-deficit, conduct, and mood disorders. **PURPOSE:** To identify trends in psychiatric diagnoses in privately-insured children prescribed atypical antipsychotics. **METHODS:** We conducted a retrospective cohort study of WellPoint claims data for children 2-18 years of age who were prescribed medications between January 2002 and March 2005. WellPoint is the Blue Cross Blue Shield licensee for the state of Missouri and the leading private insurance company in the state of Missouri. We used chi-square or Fisher's exact tests for statistical comparisons. **RESULTS:** 118,614 children had a prescription filled during the study period, and 1559 children (13 per 1000) were prescribed an atypical antipsychotic, most commonly risperidone (58%). Children prescribed atypical antipsychotics were 64% male and had a mean age of 11 years (SD ±5 years). 61% had at least 1 health care encounter coded as disruptive behavior disorder (attention-deficit or conduct disorder), 58% had a diagnosis of mood disorder (bipolar disorder or depression), 11% had a diagnosis of pervasive developmental delay or retardation, and 7% had a diagnosis of psychotic disorder. 33% (509) of children had a diagnosis of both disruptive behavior and mood disorder. No psychiatric disorder was coded for 164 (11%) children. Males on antipsychotics were 2.6 times more likely to have a diagnosis of disruptive disorder (95% CI 2.1, 3.2), and females were 1.5 times more likely to have a diagnosis of a mood disorder (95% CI 1.2, 1.8). Children ages 10-14 years were 2.4 times more likely and children 15-18 years were 5.4 times more likely to have a mood disorder than 5-9 year olds (95% CI 1.8, 3.4; 4,7.4). Children 5-14 years old were 2.2 times more likely to have disruptive disorder than children 15-18 (95% CI 1.8, 2.8). Potential neurologic side effects included 3 cases of akathisia and 1 case of dystonia with no cases of tardive dyskinesia or neuroleptic malignant syndrome. Children on atypical antipsychotics were 11.3 times more likely to have akathisia than children not prescribed these medications (95% CI 3, 38). **CONCLUSIONS:** The rate of atypical antipsychotics use in privately-insured youth appears to be similar to that in a Medicaid population (13 per 1000). Disruptive behavior disorders are the primary diagnoses in youth on atypical antipsychotics. Given the extensive use of these medications, controlled trials with long-term follow-up are critical.

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### EFFECT OF ANTIBIOTICS ON POSTNATAL INTESTINAL COLONIZATION IN TERM NEWBORNS

R Turcu, T L. Marsh, M Patterson, W Khalife, S Omar, Michigan State University, E. Lansing, MI

**Background:** The intestinal tract of the fetus is sterile but after birth is colonized with bacteria from the mother and environment. Multiple factors affect the postnatal colonization of the GI tract. Early exposure of newborn infants to antibiotics may be associated with disturbances in the normal postnatal acquisition of the intestinal flora. Most of the previous studies used classical culture methods that only identify a limited number of bacterial species. Recently, the use of molecular techniques has greatly improved the study of GI ecology. **Objectives:** This is an ongoing descriptive study designed to examine the effect of antibiotic exposure on the postnatal intestinal bacterial colonization of term newborns, by using comparative analysis of clone libraries of 16S rRNA genes. **Methods:** We plan to enroll a total of 20 infants GA>37, divided in 2 groups: antibiotic-treated (7 day course) and non-treated (control) infants. Stool samples are collected from each infant on day 3-5, day 7-10 and day 20-30 of life. DNA is amplified using universal bacterial primers. PCR products are cloned and for each sample, a library of about 96 clones is obtained. **Results:** To date, we have collected 43 stool samples from 15 infants (8 study patients and 7 controls). Clone libraries from 19 samples are available so far. Our preliminary results show that Lactobacillus, Enterobacteria or Enterococcus dominate early colonization of control infants (in one infant 63% of the clones were Lactobacillus, in 2 infants 75% and 81% of the clones were Klebsiella and Escherichia, respectively, and in 2, Enterococcus clones were isolated in 56% and 95% respectively). By day 7-10 intestinal flora was more diverse and included Enterobacteria, Clostridia, Steptococcus and Enterococcus (with no one dominating). By day 20-30 there was again an increased predominance of Enterobacteria but other species were also present. Infants exposed to antibiotics (2 analyzed to date) had a less diverse intestinal flora on the initial sample, dominated by either Lactobacillus or Bacteroides. At 7-10 days, the flora was dominated by Enterobacteria (90%). By one month of age, the number of species identified increased similarly to infants that were not exposed to antibiotics. **Conclusion:** Our preliminary observations suggest that early exposure to antibiotics may be associated with decreased diversity of intestinal bacterial colonization. As known, there is a relative paucity of bacterial species in the initial intestinal colonization of newborns. The number of species decreases further during and after antibiotic treatment. By one month of age the flora is again more diverse. As our sample size increases, we anticipate further clarification of the effect of antibiotic treatment and other perinatal factors in modifying the stool bacterial ecology.

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### METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) IN HEALTHY CHILDREN: RISK FACTOR (RF) ANALYSIS AND PULSED FIELD GEL ELECTROPHORESIS (PFGE) OF COLONIZING AND INVASIVE STRAINS.

EA Thorell, MA Jackson, C Harrison, R Selvarangan, Children's Mercy Hosp, University of MO-Kansas City Sch of Med, Kansas City, MO.

**Background:** *Staphylococcus aureus* (SA) disease is common in colonized persons. The number of patients with MRSA colonization/infection increased from 443 to 736 in our institution from 2004 to 2005. MRSA infection has become a common consultation. Recent national studies have documented SA carriage 26-36% and MRSA 0.8-9%.

**Methods:** We prospectively studied nasal MRSA carriage from 5/05-3/06 in children at an urban clinic (Site A: mainly Medicaid) or urgent care (Site B: mainly private payer). We reviewed RFs (daycare, prior antibiotic, hospitalization, skin disorders, needle use/tatoo, chronic illness, team sport participation, and healthcare exposure) of patients and their household contacts. Both anterior nares were swabbed and transport media was used. Swabs were plated on standard media. SA was identified by Staphaurex latex test. Susceptibilities were performed by automated micro-broth dilution. Invasive MRSA isolates were collected for 6 months and RFs were documented from chart. All MRSA strains were typed by PFGE.

**Results:** Nasal swabs were obtained from 377 children; 44% girls; median age 4.9 years (3m-12y). Overall, SA was identified in 98 (26%), 10 (2.7%) were MRSA; colonization rates peaked in August. Site A patients had a lower rate of SA colonization, but a higher rate of MRSA. Compared to methicillin susceptible SA, MRSA were more often clindamycin susceptible and erythromycin resistant. No single RF statistically predicted MRSA carriage from children or their contacts. RF analysis between the invasive MRSA group (n=31) and the colonized group did not show a statistical difference. PFGE typing confirmed invasive and colonizing strains to be USA 100 or 300 without predominance.

**Conclusion:** MRSA nasal carriage rates were lower than expected, especially given increasing clinical MRSA disease. Risk stratification did not predict MRSA carriage or invasive disease, but N was small. PFGE types were consistent with national data.

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### HOW CLOSE ARE WE TOWARDS ACHIEVING THE BREAST FEEDING GOALS IN THE HEALTHY PEOPLE 2010 OBJECTIVE?

HB Srinivasan and G Srinivasan, Sinai Children's Hospital, Chicago, IL.

**BACKGROUND:** Breast feeding goals for the United States are well defined. Successful long term breast feeding depends on a successful start. Healthy People 2010 breast feeding goals includes 75% of mothers initiating breast feeding. Wide differences exist in the breast feeding initiation rate amongst the various racial and ethnic groups in the US. **OBJECTIVE:** To document breast feeding initiation rates (defined as an infant receiving any amount of breast milk while in hospital after birth) in an inner city hospital serving a predominantly Hispanic and black population with low socio-economic status and poor educational background. **DESIGN/METHODS:** All healthy infants delivered at Sinai Children's Hospital room-in with their mothers in the mother-baby unit. A dedicated lactational consultant meets with the mothers following delivery and explains the importance of breast feeding and provides all technical and educational support for a successful breast feeding initiation. Data on breast feeding initiation rate for the various racial groups was prospectively collected for a one year period from July1st 2004 to June 30th 2005. **RESULTS:** During the study period, 3664 infants were delivered at Sinai Children's Hospital. 440 infants were admitted to the Neonatal Intensive Care Unit. The remainder of 3324 infants roomed in with their mothers and formed the study population. 2110(65.4%) infants were Hispanic, 1060 (32.9%) were black and 54 (1.7%) were white. The overall breast feeding initiation rate for this population was 68%. The distribution of the breast feeding initiation rate for the various racial groups is shown in the table. **CONCLUSIONS:** Breast feeding initiation rate for the black population is well below the national average and well short of the goals set forth for breast feeding in Healthy People 2010. Strenuous public health efforts are needed to improve breast feeding behaviors particularly among the black women and socially disadvantaged groups.

| | Breast Feeding Initiation Rates | | |
|---|---|---|---|
| Racial Groups | Total number of infants | Number initiating breast feeding | Percentage |
| Hispanic | 2110 | 1646 | 78 |
| Black | 1060 | 508 | 48 |
| White | 54 | 39 | 72 |

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### PREVALENCE OF MACROLIDE RESISTANT GROUP A STREPTOCOCCUS (GAS).

AL Myers, MA Jackson, R Selvarangan, S Simon, Children's Mercy Hospitals and Clinics, University of MO-Kansas City School of Medicine, Kansas City, MO.

GAS pharyngitis is a common childhood infection. Resistance to penicillin has not been documented and penicillin V is the drug of choice unless the patient is allergic. Macrolides are an alternative choice for the penicillin allergic patient, but azithromycin is often used for convenience and palatability. Macrolide resistance appears to be increasing in the United States. A surveillance study of GAS resistance was performed to determine our local resistance rates particularly since local outbreaks of pertussis in 2004 and 2005 prompted an increase in macrolide use, which might contribute to increased resistance. 200 isolates have been collected from site A and 144/200 from site B from 10/05 - 7/06. Children's Mercy Hospital was designated as site A, and a community pediatric office, with a high rate of pertussis, as site B. Isolates were cultured, and erythromycin (EES) resistance was determined by Double disk diffusion (D-test) and E-test for MIC values. Chart review identified treatment and demographic data including: age, sex, race, and payor status. Comparisons were made between the 2 sites using confidence interval analysis. Fisher's exact test was used to compare data from previous surveillance of GAS resistance in 2002 at site A to current resistance at site A and site B. EES resistance was found in 7 (3.5%) at A, and 8 (5.6%) at B, CI range -0.66-0.025. Inducible resistance was noted in 43% and 37.5% respectively. PFGE studies for genetic clones are pending. There was no difference in age, sex, or payor status between site A and B with median age of 6 yearrs (range 1 to 17), 54% male, and >50% Medicaid recipients. An AA predominance was found at site A, 47% vs 8.3 % at site B. There was no difference in treatment choice between the 2 groups, with 87-90% receiving PCN or amoxicillin. A previous surveillance study of 100 isolates in 2002 revealed no resistance at site A. A statistically significant difference in comparison with current site B data, $p<0.023$ was found, and a suggestive trend of resistance was noted at site A, $p= 0.058$. Macrolide resistance appears to be increasing in our community. This was most apparent at a site where local macrolide use may have been higher but an increase was noted for both sites. Continued surveillance may impact future antimicrobial treatment decisions.

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### ROLE OF THE GH/IGF-I AXIS IN THE GROWTH RETARDATION OF WEAVER MICE

WG Yao[1], J Zhong[2], K. E. Bethin[2], W-H Lee[1,2] [1]Department of Anatomy and Cell Biology, [2]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN.

IGF-I is an anabolic growth factor essential for growth and development, both as a mediator of growth hormone (GH) action and as a growth factor for cell proliferation and differentiation. Although the role of the GH/IGF-I axis is established for normal postnatal growth, its functional state in neurodegenerative diseases is not fully characterized. The weaver (wv) mutant mouse is a commonly used model for studying hereditary cerebellar ataxia and provides an opportunity to study the function of IGF-I in postnatal growth during neurodegeneration. Previously, we reported that weaver mice are growth retarded and their body weights correlate with a decrease in circulating IGF-I levels, suggesting that IGF-I's endocrine function is impaired in weaver mice. This study further investigated the cause of lower circulating IGF-I levels. Most circulating IGF-I is synthesized in the liver under the control of GH. We found that GH levels in wv mice are reduced, but the hepatic GH receptor signal transduction pathway functions normally, because acute GH treatment increased STAT5b phosphorylation and IGF-I mRNA levels in weaver mice. To investigate whether decreased circulating GH contributes to wv mouse growth retardation, we treated weaver mice with GH for 2 weeks and found a signify cant increase in body weights and circulating IGF-I levels in weaver mice, but not in wild type mice. In summary, our results suggest that postnatal growth retardation in weaver mutant mice likely results from a dysfunction in the GH/IGF-I axis.

Key Words: weaver mice, IGF-I, GH administration