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Antibiotic Prescribing for Lower Respiratory Tract Infection

To the Editor: In his Editorial, Dr Ebell¹ discusses his opinion that antibiotics are overprescribed for acute lower respiratory tract infection. While I agree with this general opinion, I dispute his specific conclusion that the findings in the study by Little et al² show little difference in the percentage of patients satisfied among those who received an immediate antibiotic (86%), a delayed antibiotic (77%), and no antibiotic (72%).

These differences may appear small to an academic physician and may not be important to physicians practicing in a single payer system as in England. But to a physician group that is being evaluated by multiple medical insurance plans according to patient satisfaction in the competitive US market, these differences are large and may distinguish keeping and losing a contract. I suspect that you would have the prompt attention of a hospital or medical group manager if you said that the physicians could improve the percentage of patients who report that they were very or extremely satisfied with their care by 14%. Viewed in another way, the “number needed to satisfy” for immediate compared with no antibiotics is 7, and for immediate compared with delayed antibiotics is 11. Like other physicians who work in systems in which patient satisfaction surveys are used to evaluate clinician performance, I continue to struggle with meeting patient expectations vs doing the right thing.

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In Reply: I appreciate Dr Stapczynski's comments and do not discount the perverse impact that poorly designed patient satisfaction surveys linked to “pay for performance” plans may have on physician behavior. He states that the

14% absolute difference in satisfaction “may appear small to an academic physician.” Perhaps, but while I have an academic appointment at Michigan State University, I see patients 3 days a week in a small private practice, where my income depends completely on how many patients I see and whether they pay their bills. To paraphrase a recent president, I feel his pain.

Should I excise that mole because I will make more money than by simply reassuring the patient? Should I order an x-ray, because we have this expensive machine in our office and I can get paid well for (over) using it? Should I prescribe an antibiotic to boost my satisfaction ratings and therefore my reimbursement? Maybe I should give all those patients who request Viagra, Ambien, Valium, Percocet, and Darvocet all they want. Surely they will be happier, and maybe my patient satisfaction ratings will improve. Every day, all of us make decisions that balance remuneration with doing the right thing. Fortunately, the trend in pay for performance plans is increasingly toward evidence-based process measures rather than mere patient satisfaction surveys.^{1,2} If physicians can all agree to limit antibiotic prescriptions to those patients who truly need them, then perhaps over time clinicians can “retrain” patients to no longer expect an antibiotic for every sniffle and cough, and satisfaction will no longer have any association with their use. But the first step is that each clinician must commit to less inappropriate use of antibiotics, even if it means risking slightly lower reimbursement.

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RESEARCH LETTER

Helminth Infection During Pregnancy and Development of Infantile Eczema

To the Editor: The burden of atopic and inflammatory disease is escalating in developed countries, in inverse relation to infectious diseases.¹ Mechanisms by which exposure to infections may promote balanced immunological development are being explored² and trials of therapeutic helminth parasites have been initiated for asthma and inflammatory bowel disease.^{3,4} In developing countries, advocacy for deworming is increasing, and treatment with anthelmintics targeting hookworm anemia is recommended after the first trimester of pregnancy.⁵⁻⁷ During a trial⁸ to determine the effects of deworming during pregnancy on immune responses and

infectious disease incidence in infants, we noted an unexpectedly high incidence of infantile eczema. Therefore, we examined associations between maternal helminth parasites and deworming and infantile eczema.

Methods. We enrolled 103 women who were in their second trimester of pregnancy in a randomized, double-blind, placebo-controlled trial at Entebbe Hospital, Entebbe, Uganda, between June and August 2002. Immediately after randomization, participants were treated with either 1 dose of albendazole, 400 mg orally, or with a placebo tablet. All participants received albendazole and praziquantel 6 weeks after giving birth. Before treatment and at delivery, stool samples were tested for intestinal parasites and blood was tested for malaria and microfilariae. Human immunodeficiency virus status was determined at enrollment. Participants' newborns were followed up until age 15 months. Ethical approval was given by all appropriate institutions. All participants gave written informed consent for themselves and for their children.

Diagnoses were recorded for each illness episode in the newborns and infants. All episodes in which diagnoses included "rash" were blindly reviewed. Infantile eczema was defined by a pruritic rash that was dry, excoriated, and in the typical infantile distribution on cheeks or the outer surfaces of limbs or trunk.

Associations between infantile eczema and maternal helminth infections were assessed using χ^2 tests for proportions with any event, rates to the first event, and rates including all events. Clustering effects and adjustment for potential confounding with maternal age, gravidity, and education were examined in a Poisson random-effects regression model. The effect of albendazole compared with placebo was examined in an intention-to-treat analysis. The sample size resulted in a power of 40% to 50% to detect a rate ratio of 2.0 for the effect of albendazole. Significance was set at $P < .05$. Data were analyzed using STATA version 8 (STATA Corp, College Station, Tex).

Results. Of the participants, 53 received albendazole and 50 received placebo. There were 15 participants who were lost to follow-up or withdrew before or soon after giving birth, 1 miscarriage, and 8 perinatal deaths; prevalence was similar in both groups. There was complete follow-up for 62 (78%) of 79 infants. Follow-up and illness visits did not differ by maternal helminth infection or by treatment with albendazole.

Among the 103 participants at enrollment, helminth parasites were detected in 65 (66%) of 98 participants with complete results for stool microscopy and culture and examination of blood for microfilariae (hookworm in 38 [38%] of 101 participants with results for stool microscopy).

Table. Maternal Factors Associated With Incidence of Infantile Eczema in a Cohort of 79 Ugandan Newborns Followed Up to Age 15 Months

	No. of Episodes	Person-Years of Follow Up	Incidence Rate for All Events Per 100 Person-Years*	P Value†	Adjusted RR (95% CI)‡	P Value§
Maternal age, y						
15-24	16	47	34.1	.73	1.00	.86
≥25	10	26	39.1			
Maternal HIV status						
Negative	21	61	34.3	.61	1.00	.39
Positive	5	11	44.2			
No. of previous pregnancies						
None	2	19	10.4	.005	1.00	.04
1	14	20	69.3			
≥2	8	29	27.5			
Maternal education						
None/primary school	9	42	21.5	.02	1.00	.21
Secondary/tertiary	17	31	55.3			
Maternal helminth parasites during pregnancy/at delivery						
None/none	14	19	73.1	<.001	1.00	.08
None/any	0	2	0			
Any/none	6	4	145.8			
Any/any	5	37	13.6			
Maternal treatment with albendazole during pregnancy						
Placebo	7	36	19.6	.02	1.00	.13
Albendazole	19	37	51.4			

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; NA, data not calculable; RR, rate ratio.

*Allows multiple episodes in the same infant.

† χ^2 test for unequal rates.

‡The RR allowed for clustering of episodes in individual infants and was adjusted for maternal age, gravidity, and education using a Poisson random-effects regression model.

§Wald χ^2 test.

||Data on gravidity were not available for 4 mothers; data on helminth infection status was incomplete for 4 mothers at enrollment and 10 mothers at delivery, usually because stool samples were insufficient for culture for *Strongyloides*.

Women in each treatment group had a similar age, education, gravidity, human immunodeficiency virus status, and malaria and helminth infection prevalence at enrollment. After giving birth, hookworm was present in none of 46 albendazole-treated mothers and in 13 (32%) of 41 placebo-treated mothers; the prevalence of other helminth species was similar between the treatment groups.

Fourteen infants had eczema at least once; 9 had more than 1 episode. Risk of eczema increased for maternal gravidity of 1 (rate ratio, 6.26; 95% confidence interval, 1.08-36.19) (TABLE) and decreased with presence of maternal helminth infections during pregnancy and at delivery (rate ratio, 0.26; 95% confidence interval, 0.08-0.83). There was also an inverse association between presence of helminth infections at delivery and the proportion of infants that developed eczema (4/46 [9%] vs 9/23 [39%]; $P = .002$) and rate to first episode (8.6 per 100 person-years vs 47.5 per 100 person-years; $P = .001$). Maternal albendazole treatment was associated with higher eczema incidence than placebo (Table), but this effect was not statistically significant in the adjusted model.

Conclusions. The inverse association with helminth parasites at delivery supports a hypothesis that maternal helminth infection protects against infantile eczema. This effect might be established either in utero, or in early infancy through breastfeeding. The results are consistent with studies showing reduced responses to skin prick testing in children with helminth parasites, modified by deworming.³ The absence of a significant association with albendazole treatment could be due to limited statistical power, or could indicate only partial reversal of an effect of helminth parasites before the second trimester, or the effects of species not susceptible to treatment with albendazole.

Interpretation of the results must be considered within the limitations of small sample size, participants lost to follow-up, low statistical power, and wide 95% confidence intervals, and the post hoc decision to test this hypothesis; confirmatory studies are therefore required. However, these results suggest that public health policy makers may need to consider the detrimental as well as the positive effects of deworming. Understanding beneficial effects of helminth parasites may suggest new approaches to managing atopic disease.

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