

Characterization of Vancomycin Reactions and Linezolid Utilization in the Pediatric Population



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What is already known about this topic? Vancomycin causes histamine release via IgE-mediated (allergic) and non-IgE-mediated (red man syndrome) mechanisms. Studies estimate that 1.6% to 14% of children have vancomycin reactions of either type (not specified). Red man syndrome should not preclude further vancomycin use.

What does this article add to our knowledge? The vast majority of children have vancomycin reactions consistent with red man syndrome rather than IgE-mediated allergy. These children experience unnecessary vancomycin avoidance and linezolid use, possibly due to how reactions are documented/viewed electronically.

How does this study impact current management guidelines? It encourages careful differentiation of vancomycin reaction types and highlights how this impacts management. It cautions how current electronic medical record practices may be leading to unnecessary vancomycin avoidance and linezolid use and suggests improvements.

BACKGROUND: Red man syndrome (RMS) occurs because of non-IgE-mediated histamine release. Unlike vancomycin allergy, which necessitates the use of an alternative drug (often linezolid), RMS does not typically preclude further vancomycin use. Care should be taken to differentiate these reaction types from one another to prevent unnecessary vancomycin avoidance. **OBJECTIVE:** To characterize vancomycin reaction types in our population, and to determine whether having a reaction consistent with RMS is associated with otherwise unexplained vancomycin avoidance and linezolid use.

METHODS: We retrospectively reviewed charts for children with documented vancomycin reactions. We classified the in-hospital reactions via an objective analysis and estimated the prevalence of different reaction types. We then identified children who received linezolid over 3 years, and investigated reasons for linezolid use instead of vancomycin.

RESULTS: Of the 78 in-hospital reactions we characterized, 72 (92%) were objectively consistent with RMS, 5 we could not objectively classify (2 most likely RMS, 3 more suspicious for possible IgE-mediated allergy), and 1 was a non-RMS/non-IgE reaction. Of 60 children who received linezolid, 19 had previous

reactions consistent with RMS, which should not preclude further vancomycin. Nevertheless, only 7 of 19 (37%) had a clear explanation for receiving linezolid instead of vancomycin compared with 32 of 39 (82%) children without previous vancomycin reactions ($P < .001$).

CONCLUSIONS: The vast majority of patients had vancomycin reactions consistent with RMS. These patients are at risk for unnecessary vancomycin avoidance and linezolid utilization. We propose that this may be related to how reactions appear in the electronic medical record. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:750-6)

Key words: Vancomycin; Red man syndrome; Allergy; Hypersensitivity; Anaphylactoid; Anaphylaxis; Linezolid; Children; Electronic medical record; EMR

Vancomycin reactions have been poorly characterized in pediatrics. The few studies that have been done characterize all reactions as “red man syndrome” (RMS) and there have been no studies (adult or pediatric) estimating the prevalence of true vancomycin allergy.^{1,2} In practice though, it is essential to distinguish RMS from vancomycin allergy because the management is very different. In contrast to an IgE-mediated allergy, RMS occurs because of a direct, vancomycin-induced histamine release that is infusion rate-dependent.³⁻⁶ Decreasing the rate of infusion and antihistamine pretreatment have both been shown to significantly reduce the occurrence of RMS.^{4,6-8} Thus, because further reactions can be prevented in most cases with dosing modifications, RMS should not typically preclude further vancomycin use.⁹⁻¹² Children with true vancomycin allergy, however, must either undergo vancomycin desensitization or receive an alternative medication (often linezolid).¹³

Although there remains no standard clinical description of RMS, it is typically characterized by erythema, flushing, or pruritis of the head, neck, and upper body ± hypotension; however, symptoms such as urticaria, angioedema, nausea, and

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Abbreviations used

DRESS- Drug reaction with eosinophilia and systemic symptoms

EMR- Electronic medical record

RMS- Red man syndrome

even cardiac arrest and death have also been described.^{4,11,14-16} As such, the clinical signs and symptoms of an IgE-mediated allergic reaction to vancomycin can be indistinguishable from those of RMS.^{17,18} Furthermore, although there have been case reports of vancomycin skin testing,^{19,20} there are no validated skin or blood tests to detect vancomycin allergy.^{21,22} There are, however, certain features that can distinguish vancomycin allergy from RMS. To have an IgE-mediated hypersensitivity reaction to vancomycin, a patient must have had a prior sensitizing exposure to the drug and have preformed IgE antibodies against vancomycin. RMS, however, can—and most often does—occur during a patient's very first exposure to vancomycin.^{11,12} There have been reports of cross-reactive antigens inducing drug-independent sensitization to cetuximab and neuromuscular-blocking agents, but this is considered to be very rare and has not been reported for vancomycin.^{23,24} Another distinguishing feature is that, unlike RMS, an IgE-mediated allergic reaction would not be prevented by slowing the infusion rate or pre-treating with diphenhydramine.

We previously observed a relatively high rate of electronic medical record (EMR)-documented vancomycin reactions in our population, accounting for approximately 3% of antibiotic reactions in the general population and 15% of those in patients with cystic fibrosis.^{25,26} However, as in other studies published to date, it was not clear whether these reactions were true IgE-mediated hypersensitivity reactions, RMS, or other side effects/intolerances. We therefore sought to characterize vancomycin reaction types in our population. We then sought to determine whether patients with documented reactions consistent with RMS were receiving linezolid as an alternative to vancomycin during future encounters. It is important for providers to recognize that RMS should not typically preclude further vancomycin use. Although patients may be hesitant to try the drug again after an unpleasant reaction, use of alternative therapies should be avoided whenever possible to prevent the development of antimicrobial resistance. The alternatives may also have less favorable side effect profiles than vancomycin depending on the patient (eg, may want to avoid linezolid if underlying hematologic abnormalities, gastrointestinal symptoms, or using serotonin reuptake inhibitor).

METHODS

We selected patients 17 years or younger who had vancomycin reactions documented on their allergy lists within our medical center's EMR from January 1, 2009, to December 31, 2011. We then retrospectively analyzed the details of their documented vancomycin reactions. We excluded patients with documentation of reported past reactions (36 patients) and selected those who had health care—professional observed reactions documented within 48 hours of receiving intravenous vancomycin (78 patients). To characterize the reaction types, we first determined whether vancomycin was continued the same or next day without untoward effect. If vancomycin was stopped after the reaction, we determined whether patients had ever received a

potentially sensitizing course of vancomycin before and whether they were able to tolerate vancomycin during a subsequent encounter. We then used pharmacy dispensing records from our hospital's EMR from 2009 to 2011 to estimate vancomycin reaction prevalence rates.

For characterization of linezolid utilization, pharmacy dispensing records in our hospital's EMR system were queried to identify all patients 17 years or younger who received linezolid from January 1, 2009, to December 31, 2011 (60 unique individuals among the 3 years). We performed a retrospective chart review to determine the reason for linezolid use (if multiple courses, one with the most doses administered was chosen for analysis) and we determined whether the patient had a vancomycin reaction documented on their allergy list before the linezolid use. Vancomycin reaction types were characterized as detailed in the previous paragraph. The Fischer exact test was used to compare rates of unexplained linezolid use between patients with previous reactions consistent with RMS and patients without past vancomycin reactions.

RESULTS

Vancomycin reaction patient characteristics

There were 78 individuals (39 males and 39 females) 17 years or younger who had health care—professional observed vancomycin reactions documented within 48 hours of receiving the drug intravenously. The range of reaction dates was January 16, 2009, to September 16, 2011. The patients ranged in age from 5 months to 17 years, with a median age of 10 years with an interquartile range of 9.75 years. The racial makeup was 77% whites, 8% blacks, 5% 2 or more races, 9% “other,” and 1% unknown. Eleven patients (14%) were of Hispanic ethnicity. Thirty patients (39%) had an underlying diagnosis of malignancy, and the top indication for vancomycin use was febrile neutropenia (22%). The second most common underlying diagnosis was shunted hydrocephalus (12%), with 9% of patients receiving vancomycin for a shunt infection or for shunt infection prophylaxis. See Table I for full demographic information, including the distribution of patients' ages, primary hospital services, underlying diagnoses, and vancomycin indications. The prevalence of documented β -lactam allergy was 16.7% (13 of 78), and 23.1% (18 of 78) had colonization or previous infection with methicillin-resistant *Staphylococcus aureus*.

Documented reaction characteristics

Drug reactions at our institution are documented in a specific form of the EMR to be displayed at the top of the chart. Of the 78 reactions, 58% were described by the documenting provider as RMS; 3% were entered as RMS plus another symptom (hives, eye swelling); 12% were described as rash, itching/pruritis, or hives; and 21% did not have a reaction symptom or description entered. The remaining 6 reactions (1% each) consisted of the following: flushing of the head; rash and itching; swelling of the lips, itching, and hives; oropharyngeal swelling; hemodynamic instability; and DRESS (referring to drug reaction with eosinophilia and systemic symptoms). This distribution is illustrated in Figure 1. Registered nurses initially entered 88% of the reactions, and the remaining 12% of reactions were entered by nurse practitioners, physicians, or pharmacists.

Analysis of reaction types

We used an objective step-by-step analysis to try to distinguish RMS from vancomycin allergy. First, we determined that

TABLE I. Patients' demographic characteristics

Characteristic	Children with vancomycin reactions 2009-2011	Children receiving linezolid 2009-2011
Total	n = 78	n = 60
Female sex, n (%)	39 (50.0)	28 (46.7)
Age (y), n (%)		
0-2	9 (11.5)	21 (35.0)
3-5	13 (16.7)	7 (11.7)
6-8	14 (17.9)	6 (10.0)
9-11	9 (11.5)	3 (5.0)
12-14	13 (16.7)	10 (16.7)
15-17	20 (25.6)	13 (21.7)
Race/ethnicity, n (%)		
White, not Hispanic	59 (75.6)	41 (68.3)
Black, not Hispanic	5 (6.4)	12 (20.0)
Other, not Hispanic	2 (2.6)	3 (5.0)
Unknown	1 (1.3)	1 (1.7)
Hispanic	11 (14.1)	3 (5.0)
Hospital service, n (%)		
Hematology/oncology	30 (38.4)	28 (46.7)
General pediatrics	14 (17.9)	3 (5.0)
Neurosurgery	8 (10.3)	3 (5.0)
General surgery	7 (9.0)	7 (11.7)
Pulmonology	5 (6.4)	9 (15.0)
Orthopedics	3 (3.8)	0 (0)
Cardiology	3 (3.8)	1 (1.7)
Intensive care	1 (1.3)	4 (6.7)
Other	7 (9.0)	5 (8.3)
Major underlying diagnosis, n (%)		
Malignancy	30 (38.4)	28 (46.7)
Shunted hydrocephalus	9 (11.5)	4 (6.7)
Cystic fibrosis	4 (5.1)	5 (8.3)
Congenital heart disease	3 (3.8)	1 (1.7)
Seizure disorder (without shunt)	3 (3.8)	0 (0)
Short gut syndrome	1 (1.3)	3 (5.0)
Prematurity (without above)	0 (0)	4 (6.7)
Other	8 (10.3)	4 (6.7)
None	20 (25.6)	11 (18.3)
Reason for vancomycin or linezolid use, n (%)		
Febrile neutropenia (without other)	17 (21.8)	8 (13.3)
Bacteremia or sepsis	15 (19.2)	24 (40.0)
Skin or wound infection	11 (14.1)	1 (1.7)
Respiratory infection	8 (10.3)	16 (26.7)
Shunt (infection or prophylaxis)	7 (9.0)	4 (6.7)
Abscess	4 (5.1)	2 (3.3)
Other procedural prophylaxis	3 (3.8)	0 (0)
Rule out meningitis	3 (3.8)	0 (0)
Urinary tract infection	0 (0)	3 (5.0)
Other	7 (8.9)	2 (3.3)
Unknown	3 (3.8)	0 (0)

55 patients' vancomycin courses were continued the same or next day after the documented reaction with no further symptoms, ruling out a true allergy. We then determined that it was the first-ever course of vancomycin for 16 of the 23

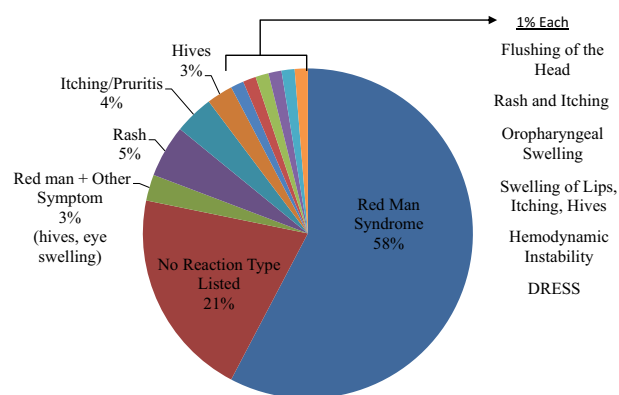


FIGURE 1. Vancomycin reaction symptoms as entered by the documenting health care professional.

remaining patients. One of these 16 patients had a non-RMS/non-mediated reaction (DRESS), and we classified the other 15 patients' reactions as RMS because of their presumed lack of previous sensitization/preformed IgE (please see Discussion for consideration of how we made these determinations and potential limitations with this step). One of the 15 patients also received vancomycin at a subsequent encounter without reaction, confirming the RMS classification. For the remaining 7 patients, we determined that 2 were able to tolerate vancomycin during a subsequent hospitalization, ruling out a true allergy. The flow-chart seen in Figure 2 depicts our analysis. Thus, we found that 72 of 78 patients (92%) had reactions most consistent with RMS, 1 of 78 (1%) had DRESS, and 5 of 78 (6%) had reactions we could not objectively identify as being consistent with RMS versus an IgE-mediated allergic reaction.

Of the 5 patients we could not classify (reactions with blue text in Figure 2), 2 most likely had RMS (documented as "flushing of the head" and "red man syndrome" in the chart), but this could not be determined objectively because they had received vancomycin earlier, the medication was stopped after reaction, and it has not been given again at our institution. The third patient was a 5-year-old boy who had RMS with an initial course of vancomycin (no symptoms upon slower infusion). He required a second course 21 days later for bacterial tracheitis, and approximately 1 hour into the first dose (being infused over 2 hours) he developed an erythematous rash from his face to his upper thighs, tachycardia (heart rate 170s), and fever (40.5°C). Eight hours later, he developed systolic blood pressure as low as 71 mm Hg requiring dobutamine. No other infection was identified at that time (negative blood cultures, urine culture, and chest x-ray). The fourth patient was a 12-year-old boy with endocarditis who initially received 7 doses of vancomycin without reaction and then was changed to nafcillin. After 21 days, he switched back to vancomycin, and with the first dose of this second course he experienced a full-body, pruritic, erythematous rash with associated wheezing. The fifth patient, a 15-year old boy with spina bifida and shunted hydrocephalus, had rash and hypotension (systolic to 70 mm Hg) while receiving a dose of vancomycin for intraoperative prophylaxis. We could not confidently determine whether he received vancomycin at an outside hospital before. To our knowledge, none of the 3 boys have received vancomycin again.

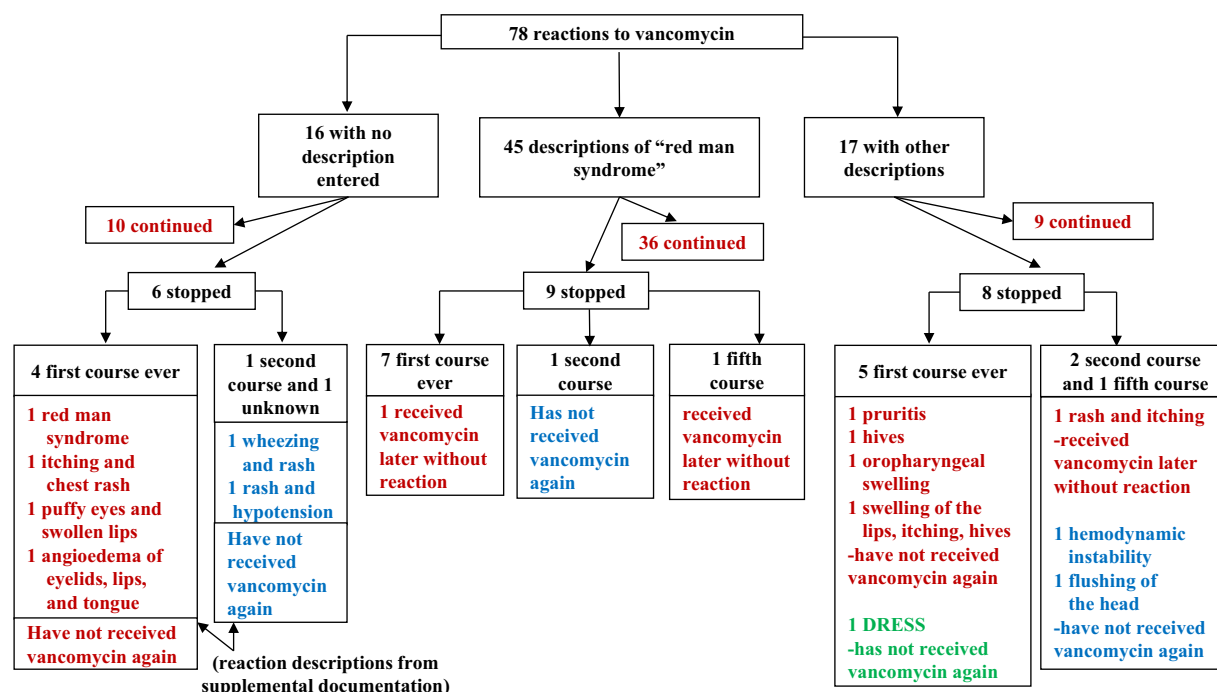


FIGURE 2. Analysis of documented vancomycin reactions. Flowchart depicting reaction descriptions as documented, whether vancomycin was continued, and whether patients received prior/subsequent courses of vancomycin. Our assessment of reaction types is denoted by colored text: red denotes consistent with RMS, blue denotes consistent with either RMS or IgE-mediated allergy, and green denotes consistent with non-RMS/non-IgE-mediated reaction.

Vancomycin reaction documentation accuracy

Of the 72 patients with reactions objectively consistent with RMS, 55 (76%) continued to receive further doses of their vancomycin course the same or next day following reaction, suggesting that many providers correctly recognized RMS and appropriately continued treatment. The concern arises, however, that if the reaction is not documented in the EMR in a way that reflects this, the patient may not appropriately receive vancomycin at a future encounter. Of those 55 patients who tolerated further vancomycin dosing, only 3 of them (5%) had EMR entries suggesting subsequent vancomycin tolerance by stating this directly, instructing to run the medication over 2 hours, or instructing to premedicate with diphenhydramine. The remaining 52 of 55 EMR entries did not mention or suggest that subsequent vancomycin was tolerated. Despite the fact that these patients continued to receive vancomycin without reaction during their hospitalization, 24 of the 55 (44%) reactions were subjectively entered as “allergy” versus side effect, adverse reaction, intolerance, and so forth.

Analysis of vancomycin reaction prevalence rates

From January 1, 2009, to December 31, 2011, there were 1346 unique individuals who received vancomycin at our institution at an age of 17 years and less. See Figure 3, A, for a graphical depiction of the vancomycin utilization by year (note that some unique individuals received vancomycin during multiple years). Twelve had vancomycin reactions documented already at the time they received vancomycin, and they were therefore excluded from the at-risk population. The prevalence of all health care—professional observed/documentated reactions

to vancomycin from 2009 to 2011 was therefore 5.8% (78 of 1334). The prevalence of RMS was 5.4% to 5.8% (72–77 of 1334), and the prevalence of vancomycin allergy was 0% to 0.37% (0–5 of 1334). The ranges are provided because we were unable to objectively classify the 5 reactions discussed, though as noted, 2 were most likely RMS and 3 were more suspicious for possible IgE-mediated allergy. The prevalence of DRESS was 0.075% (1 of 1334).

Characterization of linezolid utilization

Overall, there were 166 unique individuals 17 years and younger who received linezolid at our institution from April 21, 2004, to December 31, 2011. See Figure 3, B, for a graphical representation of the number of patients receiving linezolid by year (note that some individuals received linezolid in multiple years). We selected patients who received linezolid from January 1, 2009, to December 31, 2011, for further study and found 60 unique individuals (53% males, median age 6.5 years with interquartile range 12 years). The racial makeup was 68% whites, 20% blacks, 10% “other,” and 2% unknown. Three of the patients (5%) were of Hispanic ethnicity. There was a bimodal distribution of ages, with a peak of patients at 0 to 1 years, a low reached at 8 to 9 years, and then another peak at 14 to 17 years. We think this is likely due to the natural age distribution of the underlying diagnoses that led to infection of patients in those age ranges, with prematurity, shunted hydrocephalus, congenital heart disease, severe combined immunodeficiency, and leukodystrophy in the youngest children, and then malignancies developing in the young adults. Overall, the most common underlying diagnoses were malignancy (44%) and cystic fibrosis

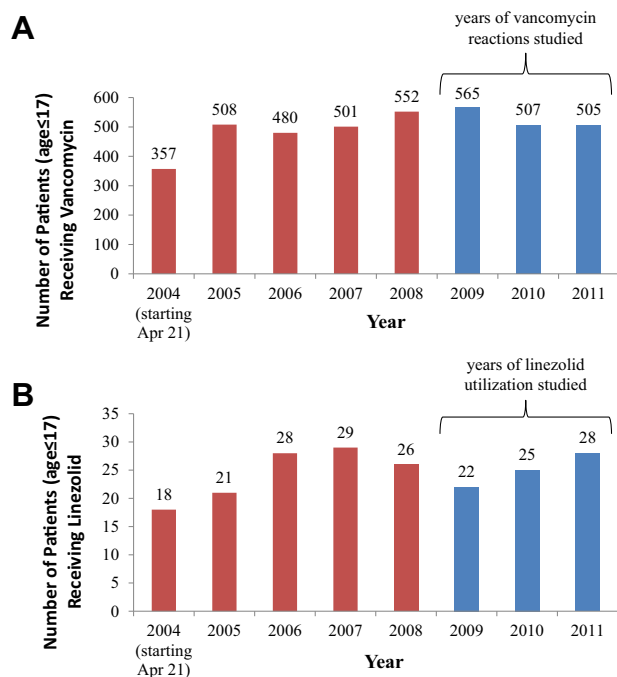


FIGURE 3. Number of children (age 17 years and younger) receiving vancomycin and linezolid by year. **A.** For each year, the number of children receiving vancomycin at our institution is shown. **B.** For each year, the number of children receiving linezolid at our institution is shown.

(8%). The most common indications for antibiotic use were bacteremia or sepsis (42%), respiratory infections (27%), empiric treatment for febrile neutropenia (14%), and shunt infection (7%). See Table 1 for full demographic information, including the distribution of patients' ages, primary hospital services, underlying diagnoses, and reasons for linezolid use.

Of the 60 linezolid recipients studied, 90% (54 of 60) had received vancomycin at our institution earlier (additional patients may have received before April 21, 2004) and 35% (21 of 60) had vancomycin on their allergy lists. Upon further analysis, it was found that 19 of 21 reactions were consistent with RMS, which should not typically preclude vancomycin use. Nevertheless, 12 of 19 (63%) were started on linezolid rather than vancomycin without a clear explanation aside from having the documented vancomycin reaction (2 required oral medication, 4 switched because of coverage concerns, and 1 declined vancomycin because of concerns it would cause excessive stooling). At the time of linezolid dosing, those 12 reactions were listed as follows: 9 RMS (6 subjectively entered as "allergy"), 1 hives (allergy), 1 rash (side effect), and 1 had no reaction symptom listed (allergy). None of these patients had evidence of a vancomycin-resistant infection, and only 1 had a history of vancomycin-resistant enterococci. In contrast, of the 39 patients without documented vancomycin reactions, 8 were being treated for vancomycin-resistant enterococci, 7 required oral medication, 13 were on linezolid due to coverage concerns, 4 for renal concerns, and only 7 of 39 (18%) did not have a clear explanation for being started on linezolid rather than vancomycin ($P < .001$ compared with those with reactions consistent with RMS).

DISCUSSION

To our knowledge, our study is the first to attempt to objectively distinguish IgE-mediated vancomycin reactions from RMS reactions and to provide an estimate of IgE-mediated vancomycin allergy prevalence. We found that the vast majority of reactions in our population could be objectively classified and were consistent with RMS (92% of reactions; prevalence, 5.4%-5.8%), whereas possible IgE-mediated vancomycin reactions were exceedingly rare (prevalence, 0.0%-0.37%). Our findings have important implications for approaching vancomycin reactions, as they suggest that the vast majority of patients with vancomycin reactions should be able to receive further vancomycin. Therefore, we suggest that providers should strongly consider readministration using a slower rate of infusion and/or antihistamine premedication after a vancomycin reaction has occurred. This should, of course, be done only in a setting in which providers are prepared to treat reactions if necessary.

In terms of how our rates compare to those of previous publications, there have been 2 studies designed to characterize RMS in pediatrics. Levy et al¹ retrospectively found that RMS occurred in 11 of 650 children (1.6%). The authors labeled all reactions as RMS, but this was not determined objectively because only 5 of 11 children were readministered the drug (all 5 tolerated), and the authors did not comment on whether patients had received prior or subsequent courses of vancomycin. More recently, Myers et al² published a study with both retrospective and prospective components that found that RMS occurred in 77 of 546 children (14%). Of note, 34 of 77 patients had received vancomycin earlier, raising the possibility of IgE-mediated reactions; however, the authors subjectively labeled all reactions as RMS and did not discuss whether the patients were able to receive further vancomycin. There have been very few adult or pediatric publications regarding IgE-mediated allergic reactions to vancomycin, but at least 11 suspected cases (1 pediatric) and various desensitization protocols have been reported.^{17,19-21,27-36}

RMS should not typically preclude further use of vancomycin; yet, we found that patients with documented vancomycin reactions consistent with RMS were significantly more likely to have unexplained linezolid use than patients without documented vancomycin reactions ($P < .001$). To our knowledge, this is the first time a link between RMS and increased linezolid utilization has been investigated. Notably, 9 of the 12 (75%) patients with unexplained linezolid use had a vancomycin reaction label of "red man syndrome," suggesting that initial recognition of a patient's reaction as RMS versus an allergic reaction is not the primary issue. This is supported by the fact that 76% (55 of 72) of patients with reactions consistent with RMS continued to receive further doses of vancomycin the same or next day following their initial reactions, suggesting that many providers correctly recognize RMS and know to continue vancomycin. Instead, we propose that the issue of inappropriate vancomycin avoidance at subsequent hospital encounters may be due to how the reactions are documented, viewed, or interpreted in the EMR.

It is important to document RMS so that proper precautions can be taken with dosing; however, there is a possibility that future providers will see vancomycin listed as a medication reaction, or get an alert when trying to order vancomycin, and not review additional information (eg, the reaction symptom, reaction type classification, or any comments). This is one

possible explanation as to why even patients with “red man syndrome” reactions listed received linezolid instead of vancomycin. Alternatively, even if providers see a reaction symptom of “red man syndrome,” they may be hesitant to order vancomycin unless there is a clear indication that it was tolerated with dosing modifications and/or that patients are willing to receive it again. Of 55 patients who continued to receive vancomycin at the time their reactions were documented, only 3 (5%) had entries implying continued tolerance of the medication. To further complicate the decision for subsequent providers, 24 (44%) had their reactions subjectively documented as “allergy” despite their continued tolerance of vancomycin. Of the children receiving linezolid without explanation, 9 of 12 had reactions subjectively listed as “allergy,” suggesting that this may have played a role in discouraging providers from ordering vancomycin. We would recommend that continued tolerance and necessary precautions (if applicable) be included with the reaction symptom, which is generally the most visible field in alerts and auto-populated text in most EMRs (eg, reaction symptom entered as “red man syndrome-tolerates run over 2 hours”).

Our study had several potential limitations. Although our estimated RMS prevalence of 5.4% to 5.8% falls between that of Levy et al (1.6%) and Myers et al (14%), it is closer to the solely retrospective study by Levy et al. Ours is likely a low-end estimate because reactions may have gone unnoticed or undocumented in our population. The retrospective nature of the study also prohibited us from questioning patients/caregivers directly about prior vancomycin usage. It being a patient’s first course ever of vancomycin was the sole evidence used in our objective classification of 14 reactions as RMS. We are confident that the patients in question had not received vancomycin earlier because most reported no previous emergency/inpatient encounters (which is likely more reliable in this age group than in adults) and because those patients who did have more complex medical histories had seemingly received all of their care within our system and had detailed records of any medical changes/events. The determination was based on an exhaustive review of notes/scanned in documents and secondary check with automated chart searches. Nevertheless, it is possible these patients could have received vancomycin during outside encounters that went unreported to our providers, but this information was used for the objective classification of only a small number of the reactions. In addition, the retrospective design prohibited us from asking about maternal vancomycin use during pregnancy or breast-feeding, which theoretically could have led to patient sensitization/IgE formation, but this has not been reported before and vancomycin (category C) is not typically given in pregnancy or while nursing unless absolutely needed.

A further consideration in our classification of the 14 first-ever course of vancomycin reactions as RMS is whether one could have sensitization to vancomycin without previous drug exposure. With the discovery of reactions to first-ever doses of cetuximab due to preformed anti-galactose- α -1,3-galactose and reports of pholcodine causing increases in IgE antibodies associated with allergy to neuromuscular-blocking agents, this is certainly a consideration, but we have not heard of any suspected cases involving vancomycin.^{23,24} Finally, the prevalence of vancomycin reaction types and the higher rates of unexplained linezolid use in patients with RMS may be related specifically to our population, providers, or EMR. Further studies are necessary to investigate the generalizability of our results.

In conclusion, our study found that the vast majority of reactions in our pediatric population were objectively consistent with RMS, whereas reactions consistent with true, IgE-mediated allergic reactions were extremely rare. RMS should not typically preclude further vancomycin use, and providers should strongly consider whether vancomycin can be readministered with dosing modifications. Nevertheless, we found a significantly higher rate of unexplained vancomycin avoidance and increased linezolid use in patients with documented reactions consistent with RMS. We suggest that this may be related to how vancomycin reactions are documented, viewed, or interpreted in the EMR. Our findings highlight the importance of complete/accurate vancomycin reaction documentation, including whether further vancomycin was tolerated. Providers should carefully review and interpret the details of vancomycin reactions before an alternative antibiotic is selected. Finally, our project suggests system-wide changes in how medication reactions are documented and viewed in the EMR could promote antimicrobial stewardship and, in some cases, could lead to improved patient care.

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