Ann Allergy Asthma Immunol xxx (2016) 1–6

Contents lists available at ScienceDirect

Perspective

Redesigning the allergy module of the electronic health record

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ARTICLE INFO

Article history:
Received for publication April 19, 2016.
Received in revised form May 16, 2016.
Accepted for publication May 19, 2016.

Introduction

Adverse drug reactions (ADRs) are a major cause of morbidity in modern health care,[1,2] with 20% to 35% of patients reporting 1 or more ADRs.[3,4] Some ADRs warrant entry into the electronic health record (EHR) to inform future prescribing and prevent recurrence. This clinical documentation is typically placed in the allergy section of the EHR. Although this section is termed *allergy*, only a few of the reactions are immunologically mediated, with even fewer mediated through antigen-specific IgE (ie, classic allergy). Widespread overuse of the term *allergy* makes patients, and even health care professionals, think that anaphylaxis could occur with reexposure or that desensitization is an appropriate management plan.

Although the allergy section of the EHR was designed to improve patient safety, it is currently failing to do so.[5,6] Routine, inconsequential warnings can result in all warnings being ignored; alarm fatigue has been previously observed with biomonitors in the intensive care unit.[7] Allergy alerting has been similarly affected; prior estimates indicate that a clinician would need to review more than 100 allergy alerts to identify one that could prevent an adverse drug event, and alerts are overridden by health care professionals 90% to 95% of the time.[5,6,8] To reverse this trend and make the allergy field a useful tool, substantive changes in EHR design and clinician documentation are required. In this perspective, we aim to envision and describe a redesigned allergy module that could use EHR patient data and interactive decision support to provide clarity of assessments and rational management recommendations for patients with a variety of drug intolerances.

Common Drugs and Reactions

Although ADRs can happen with any drug, a relatively short list accounts for most allergy entries.[3,4] The most frequently reported allergies are to antibiotics, opiates, nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors, other antihypertensive agents, lipid regulators, radiocontrast agents, antiepileptics, antidepressants, corticosteroids, stimulants, and local anesthetics.[3,4] However, although these drug classes represent most entries, most EHRs do not support their ease of entry with a “quick pick” or “quick entry” list but instead require the health care team to find these agents undifferentiated from a comprehensive alphabetical drug dictionary.

For these and other drug classes, there are commonly identified reactions seen in clinical care. Many of the most common reactions do not preclude future use of the drug. Using a few drug class examples, we illustrate the clinical importance of the most common drugs and their most common reactions.

Penicillins

Penicillins are the most commonly reported drug allergy, but when patients reporting penicillin allergy are evaluated by allergists/immunologists, less than 5% are truly allergic.[9,10] An unverified EHR report of penicillin allergy is not benign; these patients have more morbidity and use more health care resources than patients without this label because of the prescribing of more broad-spectrum, suboptimal, or more toxic antibiotic therapies.[6,11,12] The most common reaction to penicillins is a delayed benign maculopapular rash. Although this reaction should be entered into the allergy section and is often immunologic, rechallenge of penicillins under medical observation would be appropriate if penicillins were needed in the future.[10,13–15] Although this management plan is based on common allergy

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Disclosures: Dr Blumenthal reported creating clinical decision support for drug allergies used within Partners HealthCare Systems. Dr Macy reported being a partner in the Southern California Permanente Medical Group, receiving research grants from ALK Abello Inc to study adverse drug reactions, and being a member of clinical trial safety and monitoring committees for BioMarin Pharmaceutical Inc and Ultragenyx.

http://dx.doi.org/10.1016/j.anai.2016.05.017

specialist knowledge,[10,16] general medical professionals generally lack this knowledge. Thus, an intelligent EHR allergy module could serve to prevent unnecessary use of alternative antibiotics that lead to untoward outcomes in penicillin allergy.

Opiates

Opiates, another commonly reported allergy, cause gastrointestinal issues (eg, nausea, constipation), central nervous system depression, and itching and rash. These reactions are all expected pharmacologic effects, none are IgE mediated, and none absolutely preclude future opiate exposures.[10,17] Immediate reactions to opiates are commonly attributable to direct mast cell activation release of histamine (ie, IgE independent). Even for severe reactions of this type, some semisynthetic opiates, such as fentanyl, can be tried. In addition, because the mechanism is not through an IgE antibody, use of the lowest effective dose and pretreatment with antihistamines are often effective to reduce symptoms. A smart EHR could recognize immediate symptoms entered to an opiate medication as IgE independent and autopopulate a management plan that includes details for safe and appropriate opiate use in the future.

NSAIDs

NSAIDs cause gastrointestinal upset and gastrointestinal bleeding, as well as rashes and angioedema. However, NSAID reactions that are seemingly allergic do not absolutely preclude future use because most reactions are also not mediated through IgE. For example, a patient with urticaria in the setting of a viral infection may have a worsening urticaria, or development of angioedema, after ingestion of a high-dose NSAID. Several months later, in the absence of acute infection, the patient may again tolerate high-dose NSAIDs. High-dose NSAIDs may be contraindicated in patients because of other acute conditions (eg, acute kidney injury, duodenal ulcer) or chronic conditions (eg, after gastric bypass surgery, chronic renal disease), but these same individuals may benefit from the cardioprotection of 81 mg of aspirin daily.[18,19] With an improved allergy module, the EHR could support differential alerting based on the patient history. For example, an order for a low-dose aspirin in a patient after gastric bypass surgery would not trigger an interruptive alert, but a patient with acute kidney injury prescribed any NSAID would result in an interruptive alert.[20]

Radiocontrast Media

Acute-onset reactions associated with nonionic or iso-osmolar radiocontrast media are much less frequent compared with reactions with old-style hyperosmolar radiocontrast. The most common radiocontrast-associated reactions include flushing, itching, and hypotension, all thought to be related to direct mast cell activation (ie, IgE independent). In patients with a history of a contrast reaction, only nonionic, low-ionic, or iso-osmolar radiocontrast should be used. Premedication regimens that include steroids and antihistamines are commonly recommended, although premedication is not as helpful in reducing reactions from nonionic or low-ionic contrast-associated reactions.[20] For individuals with a history of delayed-onset, T-cell–mediated reactions, a low-ionic or iso-osmolar contrast material from another non–cross-reacting group can be used. Non–cross-reacting groups include group A (ioxitalamate, iopamidol, iodixanol, iomeprol, ioversol, and iohexol), group B (iobitridol and ioxaglate), and group C (amidotrizoate).[21,22] The EHR could support automatic assessment and contrast management plans based on the patient's reaction history.

The Intolerance Module: Renamed and Redesigned

The allergy field should be renamed intolerances to more accurately reflect the variety of information populating this field, including patient preference, contraindications, adverse effects, and immunologic reactions (Fig 1). Although the word *intolerance* is often used to describe mild adverse effects, its meaning is literally the inability to take a drug without adverse effects and does not intrinsically convey severity. Immunologic reactions and true, IgE-mediated drug allergy would remain a small subgroup of reactions in the intolerance field.

The intolerances section would have 3 mandatory components to be entered by health care professionals: (1) drug name (or drug class if drug name is unknown), (2) approximate date of index reaction, and (3) reaction details (Fig 2). For adverse effects and possible immunologic reactions, a fourth component will be included, specifically whether the association is *suspected* or *confirmed*. Confirmation of immunologic reactions would involve appropriate testing and/or subspecialist case review.

Medication intolerance entry would have a "quick entry" list of the most common drugs with their most common reactions. Drug entry would prompt use of the specific drug name (eg, cephalexin) as opposed to the drug classes (eg, cephalosporins) whenever this detail is available. The date of the index reaction would be entered and could be used by health care systems to systematically identify patients for testing whose IgE-mediated reactions may have waned

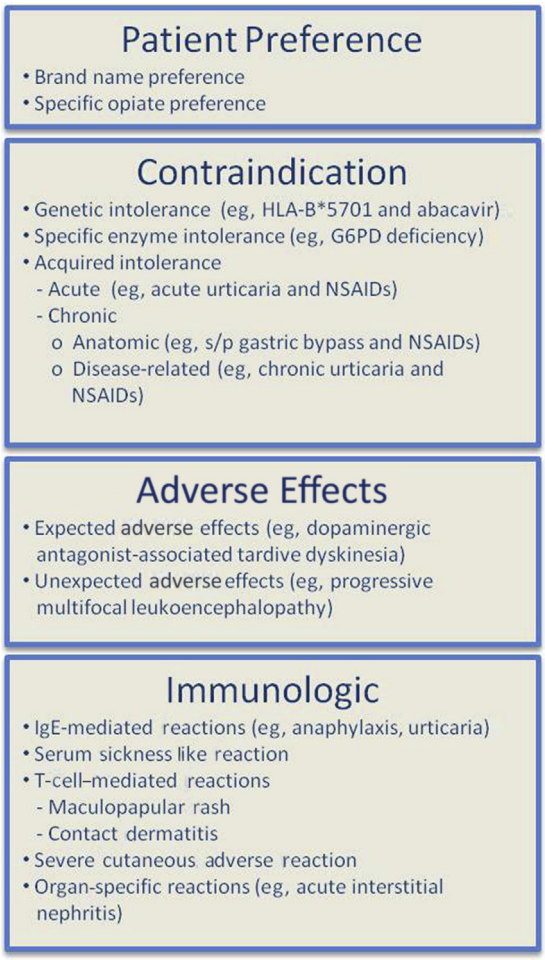

Figure 1. Proposed outline for categorization of drug intolerances. G6PD, glucose-6-phosphate dehydrogenase; NSAID, nonsteroidal antiinflammatory drug; s/p: status post.

A

Drug Name	Date of Index Reaction	Reaction Details	
		Type	Detail
Hydrocodone/paracetamol	01/01/2016	Patient preference	Prefers "oxycodone/acetaminophen"
Montelukast	09/05/1996	Patient preference	Prefers "singulair"

B

Drug Name	Date of Index Reaction	Reaction Details	
		Type	Detail
Lisinopril	12/12/2012	Contraindication	Hereditary angioedema
Abacavir	05/22/2002	Contraindication	HLA-B-5701
Succinylcholine	05/23/2009	Contraindication	Butyrylcholinesterase
Beta Blockers	05/13/2016	Contraindication	Receiving allergen immunotherapy

C

Drug Name	Date of Index Reaction	Reaction Details			Computer Generated Assessment and Management	
		Type	Detail	Suspected or Confirmed	Assessment	Management
Atorvastatin	01/01/2004	Adverse effect	Myalgia	Confirmed	Expected side effect	Avoidance Other HMG-Co-A reductase inhibitors can be tried
Captopril	04/04/2000	Adverse effect	Cough	Confirmed	Expected side effect	Avoidance Other ACE inhibitors can be tried
Coumadin	09/14/1999	Adverse effect	Bleeding	Confirmed	Expected side effect	Avoidance Caution with use of any anti-clotting factor or anti-platelet agent
Rituximab	05/17/1980	Adverse effect	PML	Suspected	Unexpected side effect	Avoidance Report to FAERS

D

Drug Name	Date of Index Reaction	Reaction Details			Computer Generated Assessment and Management	
		Type	Detail	Suspected or Confirmed	Assessment	Management
Amoxicillin	05/06/1949	Immunologic	Rash Wheezing Diarrhea	Suspected	Anaphylaxis Type 1 IgE-mediated reaction	Referral to an allergist/immunologist for penicillin skin test
Carboplatin	11/18/1979	Immunologic	Rash	Suspected	Urticaria Type 1 IgE-mediated reaction	Can be administered by desensitization only
Cefaclor	11/11/2000	Immunologic	Rash Myalgias Arthralgias	Confirmed	Serum sickness-like reaction IgG-mediated reaction	Other cephalosporins can be administered
Trimethoprim and sulfamethoxazole	05/17/1980	Immunologic	Rash	Suspected	Maculopapular Rash T-cell –mediated reaction	Can be administered under observation, if needed.
Vancomycin	11/11/2014	Immunologic	Rash Renal injury Hypotension	Suspected	DRESS syndrome T-cell– mediated reaction	Avoidance Case review by an allergist/immunologist or dermatologist Report to FAERS
Latex	01/06/1992	Immunologic	Rash	Confirmed	Contact dermatitis T-cell–mediated reaction	Avoidance Reexposure will cause delayed rash

Figure 2. Intolerances section. A, Patient preference; B, contraindication; C, adverse effects; and D, immunologic reactions. ACE indicates angiotensin-converting enzyme; DRESS, drug rash eosinophilia and systemic symptoms; HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A; FAERS, Federal Drug Administration Adverse Event Reporting System; PML, progressive multifocal leukoencephalopathy.

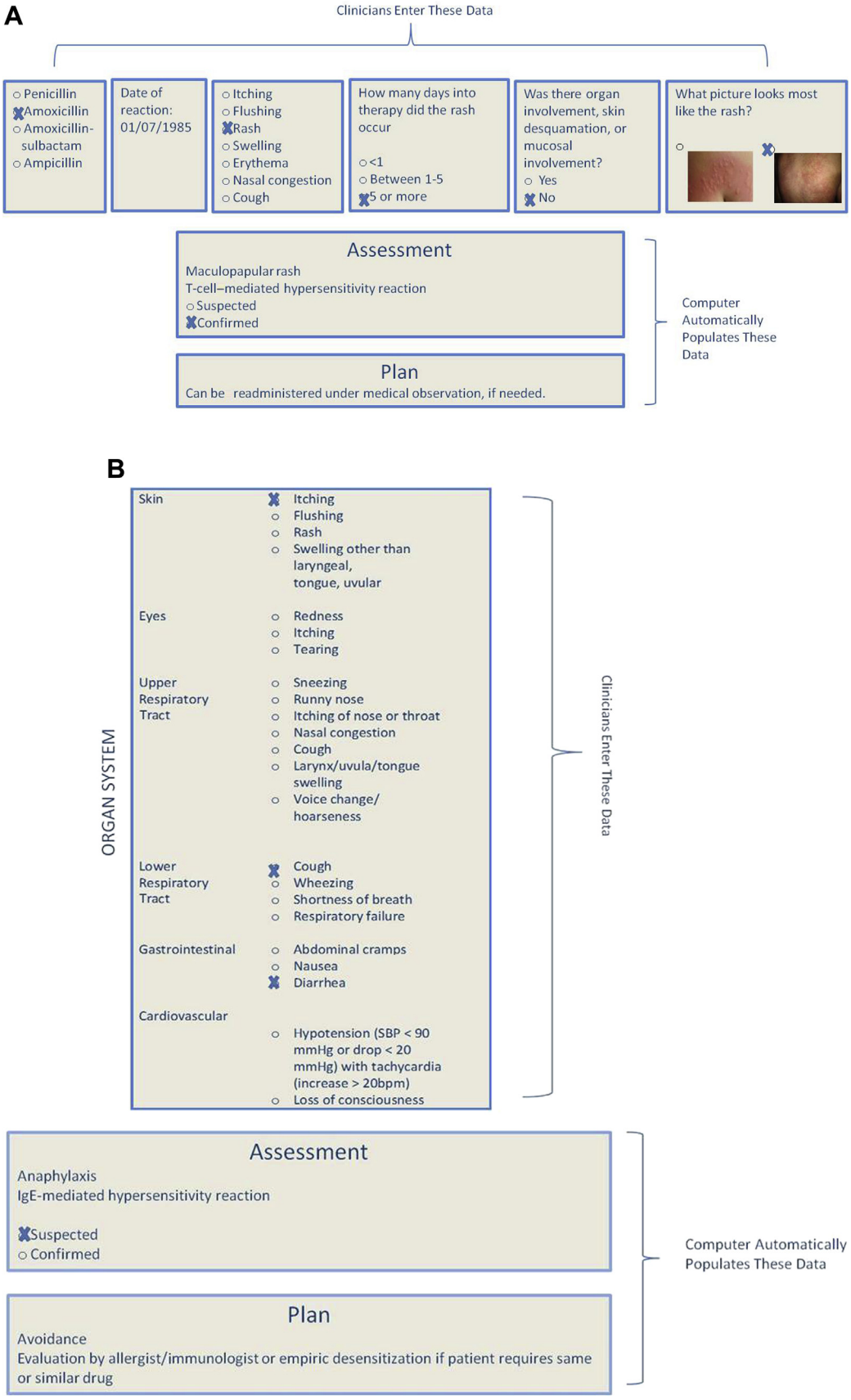

Figure 3. Examples of clinical decision support for improved intolerances module. A, Decision support for reaction to amoxicillin identified a maculopapular rash, a benign T-cell–mediated reaction. B, Use of symptom checklist identifies anaphylaxis and appropriate management plan. SBP indicates systolic blood pressure.

over time (eg, penicillin allergy testing could be flagged 10 years after the index reaction).

Inclusion of reaction details is important for future prescribing, with more detail resulting in more patients being prescribed the same or similar medication again.[23] Therefore, inclusion of reaction details would accommodate the variety of factors potentially involved in the intolerance, including patient preference, contraindications, adverse effects, and immunologic reactions. Patient preference can be a major factor in drug intolerance; patients often prefer a name product or prefer a specific opiate over another. Contraindications would be automatically identified through communication with a patient's problem list or diagnoses. For example, when a patient receives a diagnosis of glucose-6-phosphate deficiency, all medications that potentiate drug-induced anemias would automatically populate into the intolerance section as a contraindication. Similarly, if a patient has a genetic marker that predisposes him or her to a serious cutaneous adverse drug reaction (SCAR), such as to a specific antiseizure medication[24] or antiviral medication,[25] these medications would be automatically populated into the intolerance section as a contraindication. If a problem or diagnosis resolves, the intolerance would also be resolved.

Mechanisms of ADRs include adverse effects (both expected and unexpected) and immunologic reactions (ie, types 1-4 hypersensitivity reactions).[26] All commonly recognized reactions would be available for coded entry from an expanded reaction dictionary. Currently, many severe immunologic reactions, including the SCARs, acute interstitial nephritis, serum sickness–like reactions, and others, must be entered in free text. Noncoded data can compromise patient safety, and coded reaction entries would additionally allow for targeted clinical decision support for these important immunologic reactions.

Because determining drug allergy mechanism is challenging for general clinicians, the EHR would contain point-of-use clinical decision support to guide entry for possible immunologic reactions (Fig 3).[27–30] Symptom checklists and short survey questions probing patient allergy history would yield appropriate immunologic assessments. Immunologic reactions would automatically be entered as suspected. Confirmation of reaction could be targeted based on patient and health care system priorities with diagnostic evaluations and consultations, as appropriate, by allergy/immunology and/or dermatology specialists. Entry of a reported SCAR would prompt standardized scoring (eg, regiSCAR) along with subspecialist review. Prior analyses have found that less than 15% of patients coded for Stevens-Johnson syndrome (SJS, a SCAR) have SJS, and EHR allergy module report of SJS attributes SJS to more than 1 drug in more than 15% cases.[31,32] T-cell–mediated contact sensitivities to adhesives, topical antibiotics, topical anesthetics, and other potential hospital allergens would be clearly identified as topical reactions where reexposure generally causes only mild rashes. With this improved data capture related to the specifics of the drug intolerance, assessments and management plans could be automatically determined with clear and clinically useful information. Specialist input would be incorporated into the EHR intolerance module to facilitate communication between clinical care professionals and pharmacists.

With this vision and general framework (Table 1), an intolerances field in the EHR would improve patient safety, quality of care, and ease of clinical management. The word *allergy* would be reserved for IgE-mediated reactions that are amenable to desensitization when the culprit medication is needed. With the use of limited decision support, clinicians would know which situations need avoidance, which can accept reexposure, which can be overcome with premedications, and which can be desensitized. Improved and safe medication administration would be possible for millions of Americans with reported drug allergies.

Table 1
Framework for the intolerance module

Make it Relevant	• The most common drugs and reasons for drug intolerance would be listed first. • Environmental (eg, ragweed, dog dander) or venom (eg, yellow jacket, wasp) allergies would not be noted in the drug intolerance field. These would be included in the problem list or diagnoses. • Food allergens would have their own EHR territory. IgE-mediated reactions to foods are particularly important for the safety of hospitalized patients and must communicate with dietary services.
Make it Interactive and Reactive	• Intolerances would communicate with the EHR problem list or diagnoses to autopopulate contraindicated medications associated with specific conditions. The intolerances would automatically delete when the problem is resolved. • Intolerances would communicate with laboratory ordering. New suspected anaphylaxis prompts ordering of a serum tryptase and entry of latex prompts order of the commercially available antilatex IgE ELISA test. • Intolerances would connect to the FDA Adverse Event Reporting System, the nation's system for collecting adverse events data, when indicated. • Reaction detail would be required for intolerances. On demand clinical decision support would launch at the time of allergen entry for immunologic reactions to provide more accurate assessments. • Patients with select immunologic reactions amenable to testing would be automatically referred for allergy testing. • Patients with suspected SCARs would receive subspecialist case verification.
Make Pop-Up Fatigue Stop	• Alerts would use both drug and reaction details. • Although many alerts do not signal an absolute contraindication, when a drug is absolutely contraindicated, it would not be possible to administer. • Systemwide alerts that are widely ignored would be assessed annually for removal. • If an alert is overridden 3 or more times, then the intolerance would be deemed inconsequential to care and the clinician would be prompted to delete the intolerance. • If a patient carries an intolerance that is immunologically mediated and tolerates that drug in reexposure (whether purposeful or accidental), the original intolerance would be automatically removed from the EHR.

Abbreviations: ELISA, enzyme-linked immunosorbent assay; EHR, electronic health record; FDA, Food and Drug Administration; and SCAR, severe cutaneous adverse reaction.

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