Yukon-Kuskokwim HEALTH CORPORATION

# Amoxicillin Allergy-Still Stamping It Out

K Jane McClure, MD

What You Need to Know

What You Can Do to Help

GRAND ROUNDS 8/6/19

# WHAT

- Avoid adding incorrect amoxicillin allergy labels
- Remove incorrect amoxicillin allergy labels

# WHY

- Children mislabeled as penicillin-allergic have more medical visits, receive more antibiotic prescriptions, and have longer hospitalizations with more antibiotic-related complications.
- There are 3100 YKHC patients labeled as ‘amoxicillin/penicillin allergic’!!!!!!
- Research repeatedly shows that over 90% of patient amoxicillin allergy labels are incorrect.
- Amoxicillin and Augmentin are the BEST first line option for treating otitis media and pneumonia in children. Cephalosporins do not work as well against *Strep pneumo*.
- Not being able to use a penicillin limits options for appropriate, narrow-spectrum antibiotic use for OM, pneumonia, Strep pharyngitis, and Strep skin infections in all ages.
- Increased use of cephalosporins for unproven ‘amoxiciilin allergic’ patients is creating resistance.

# How Did These Patient Allergy Labels Get There??

- A large number of allergy labels were imported from RPMS to RAVEN in the EHR conversion of 2013.
- Limited patient, parent, health aide, and provider knowledge about signs and symptoms of a true amoxicillin allergy leads to ongoing incorrect allergy labeling – the “sticky diagnosis.”
- Patients and caretakers self-report amoxicillin allergy history; these reported allergies are added to the allergy list.
- Most rashes and rash histories are not reviewed for true allergy.

# Per UpToDate

- **IMPACT OF PENICILLIN ALLERGY ON CARE —**

There is morbidity, mortality, and economic cost associated with the unnecessary withholding of penicillins in patients who are labeled as allergic on the basis of history alone. Patients with a history of penicillin allergy are more likely to be treated with broad-spectrum antibiotics, such as quinolones or vancomycin. There are distinct disadvantages to broad-spectrum agents, which are often more expensive, associated with more side effects (such as *Clostridioides* [formerly *Clostridium*] *difficile* infection), and less effective for some infections.

- **STEWARDSHIP PROGRAM INTERVENTIONS—**

**Antimicrobial allergy assessment** — Antimicrobial allergy can complicate selection of appropriate antimicrobial therapy. Patients with suspected antimicrobial allergy may receive suboptimal therapy and/or broader-spectrum antimicrobial therapy than necessary.

Correcting an inaccurate antimicrobial allergy history in the medical record ("de-labeling") can be very useful for guiding subsequent decisions regarding a patient's antimicrobial therapy. Increasing numbers of hospitals are developing decision-support tools to guide non-allergists in determining when patients labeled as penicillin allergic can safely receive penicillins and related antimicrobials. In addition, beta-lactam test dose protocols (for patients with a history of beta-lactam allergy) can also be used to reduce need for alternative antimicrobial agents.

# PENICILLIN ALLERGIC REACTIONS

- Scary
- Bad
- Just Fine!

# SCARY – Immediate Hypersensitivity Reaction (Anaphylaxis)

A serious allergic or hypersensitivity reaction that is rapid in onset and may cause death

**Criterion 1** — Acute onset of an illness (usually occurs in minutes) involves skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

**PLUS one of the following**:

- Respiratory compromise-dyspnea, wheezing, stridor, hypoxemia.

OR

- Hypotension or associated symptoms and signs of end-organ dysfunction (e.g., hypotonia, syncope, incontinence.)

**Criterion 2** — Two or more of the following that occur rapidly after exposure **to a LIKELY allergen for that patient**

- Involvement of the skin-mucosal tissue-generalized hives, itch-flush, swollen lips-tongue-uvula.
- Respiratory compromise-dyspnea, wheezing, stridor, hypoxemia.
- Reduced BP or associated symptoms and signs- hypotonia [collapse], syncope, incontinence.
- Persistent gastrointestinal symptoms and signs-crampy abdominal pain, vomiting.

**Criterion 3** — Reduced BP after exposure **to a KNOWN allergen for that patient**.

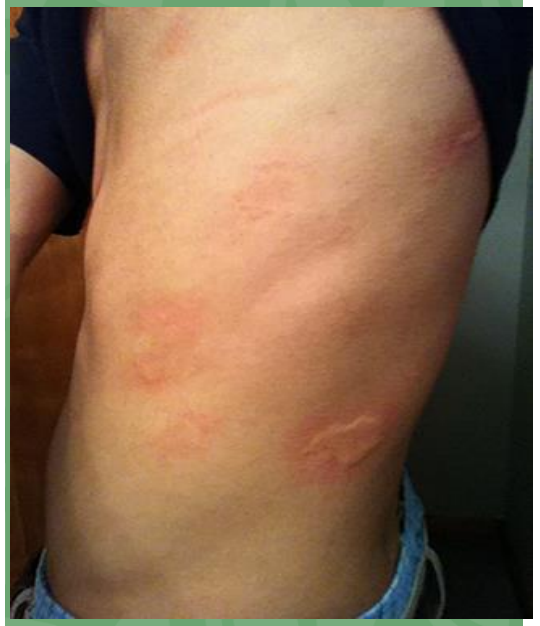
**STOP EXPOSURE----EPINEPHRINE----OXYGEN----FLUIDS----AIRWAY MANAGEMENT**

# BAD – Delayed Urticarial Eruptions (Hives)

- Hives usually begin more than an hour after the last administered dose, often 1-3 days into the course.
- Unlike anaphylaxis, these eruptions have a later onset. Other, more serious symptoms are unlikely.
- These patients should be labeled as allergic and referred to Allergy and Immunology after age five for allergy testing. It is unlikely that they are truly allergy, but they should not be given penicillin until this happens.

# Hives

Hives are raised, red (and/or pale) patches of skin that are usually very itchy. They come and go within a few hours, but they can show up again and again in some people.

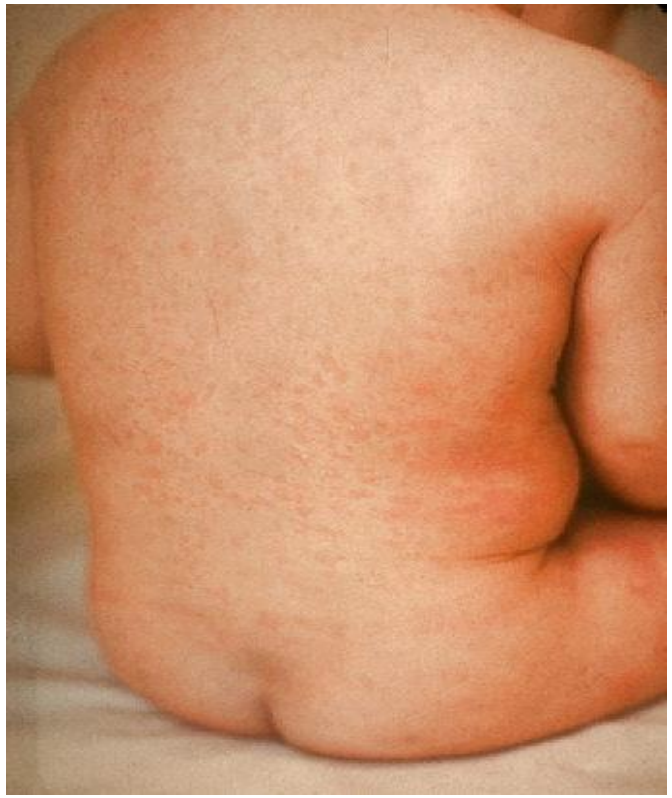


# JUST FINE!! – Delayed Cutaneous Eruption

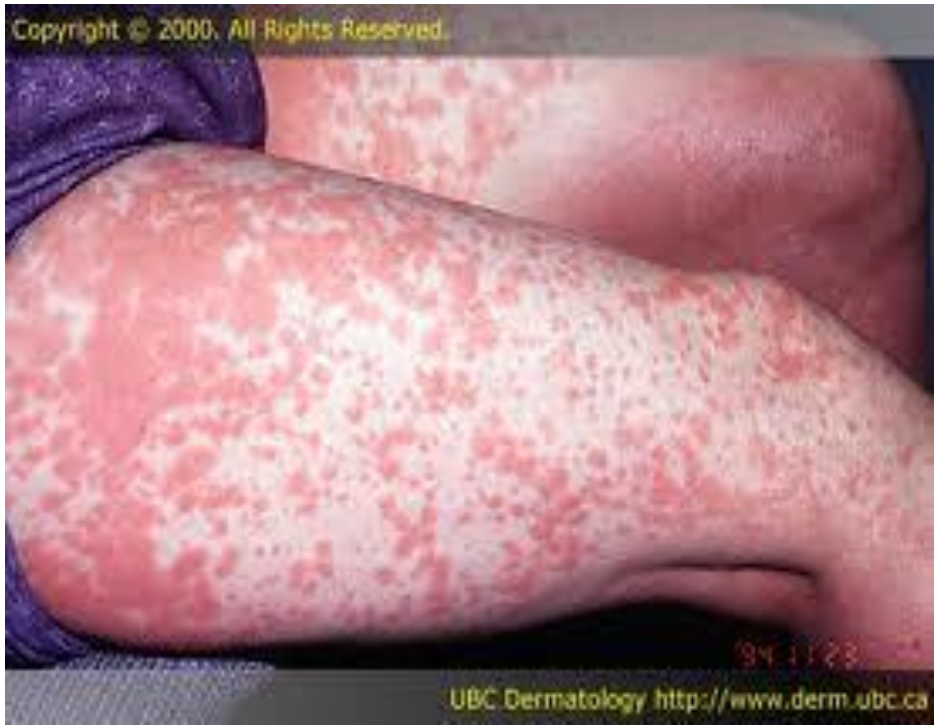
- The most common reactions to penicillins are delayed cutaneous eruptions. Most likely mediated by T-cells in the skin.
- Usually maculopapular or morbilliform and often associated with a viral infection. Occur in 3-7% of children given a penicillin.
- Pruritus may or may not be a feature.
- More prevalent in young children (usually under 12 months). This is the classic “amoxicillin rash.”
- These rashes are believed to be mediated by T-cells.

# Viral Rash Nomenclature for Documentation

## Maculopapular=flat and bumpy

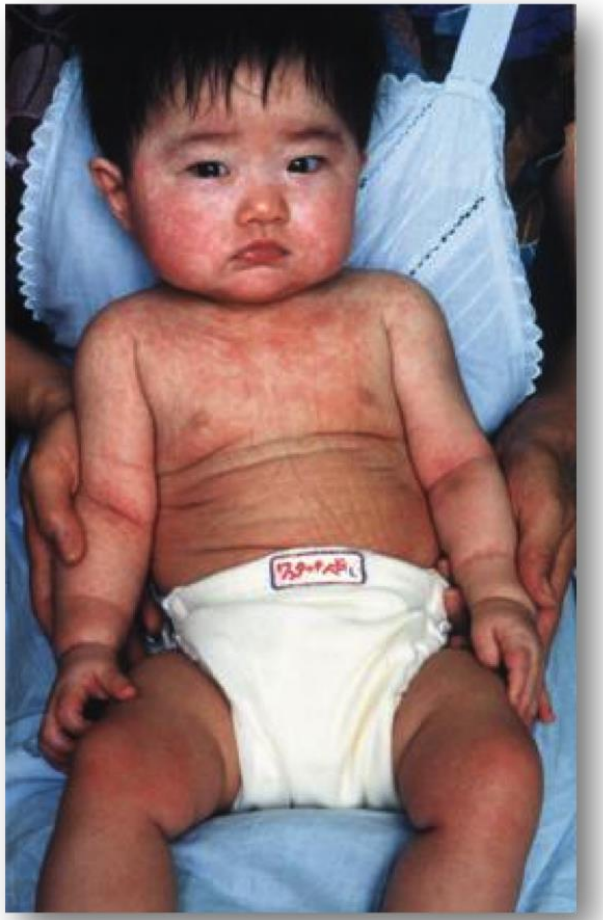


## Morbilliform=measles-like



## Hives come and go, move around and change shape

## Viral or delayed cutaneous exanthems are fixed but can expand over body over several days



# True Penicillin Allergy is Rare

- Anaphylaxis occurs in only 1-4/10,000 administrations.
- In large studies of penicillin skin testing, over 90 percent of patients are found not to have positive skin tests and are able to tolerate penicillin.
- Families are often worried that amoxicillin allergy may “run in the family.” There’s limited evidence for a genetic link.
- Referral — Referral to an allergy specialist for diagnostic testing should be considered for any patient with a history of penicillin allergy consistent with a possible IgE-mediated mechanism (the SCARY or the BAD).

# Options for treatment with penicillin after a reported non-urticarial rash (UpToDate):

- Cutaneous reactions — If a patient clearly describes a delayed-onset eruption that did not itch or involve urticaria, was not accompanied by any systemic symptoms, and did not involve blistering or exfoliation of the skin, then it can be reasonably assumed that the patient had a delayed maculopapular cutaneous reaction. **Such patients can be treated with the same or other penicillin in the future, with the recognition that such reactions may recur.**
- Safe re-administration with the same or similar drugs is well documented in children, in whom delayed cutaneous eruptions regularly occur in the setting of viral infections.
- In a study of 88 children with delayed urticarial or maculopapular rashes on beta-lactam (mostly amoxicillin) antibiotics, only 6 of 88 (7 percent) reacted again when re-challenged with the same antibiotic two months after the original reaction. The reactions were all mild and similar to the original reactions.

# Allergic Reaction Overview

**SCARY** = Immediate Type 1 IgE-mediated reactions

Hives, +/- swelling of lips/tongue/uvula, +/-respiratory distress, +/- decreased blood pressure.

**Don’t ever give drug again without allergist evaluation.**

**BAD** = Delayed cutaneous T-cell-mediated reactions

Hives without evidence of anaphylaxis.

**Refer to allergist after five years old to evaluate.**

**JUST FINE** = Delayed cutaneous reactions which account for over 90% of reported allergies.

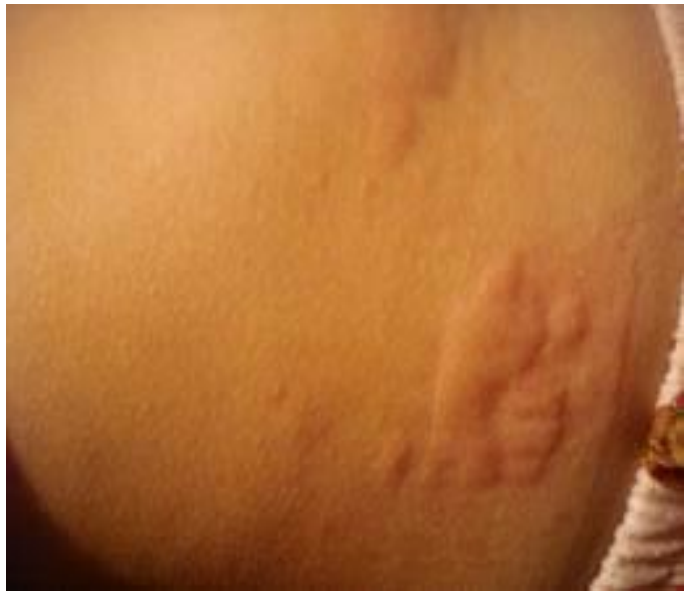
Maculopapular/morbilliform rash without evidence of anaphylaxis.

Often associated with viral infections…This is what we mostly see.

**Please try amoxicillin again!!!**

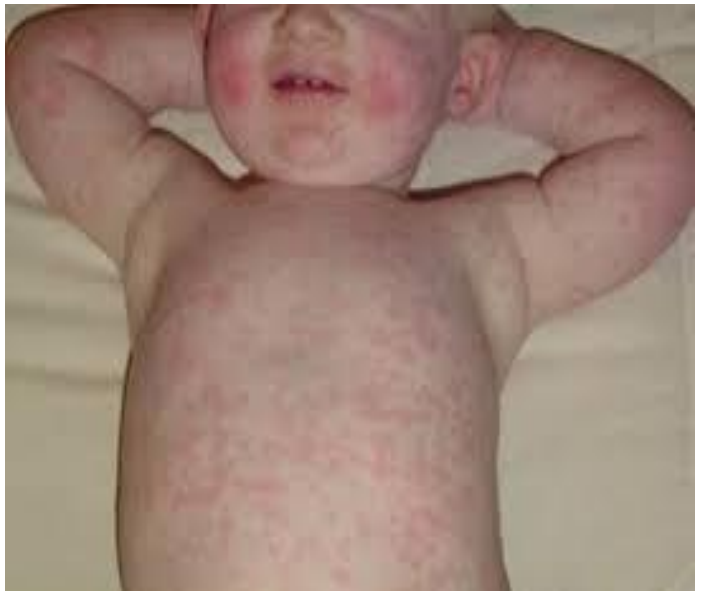
# What are these rashes?

## Anaphylaxis

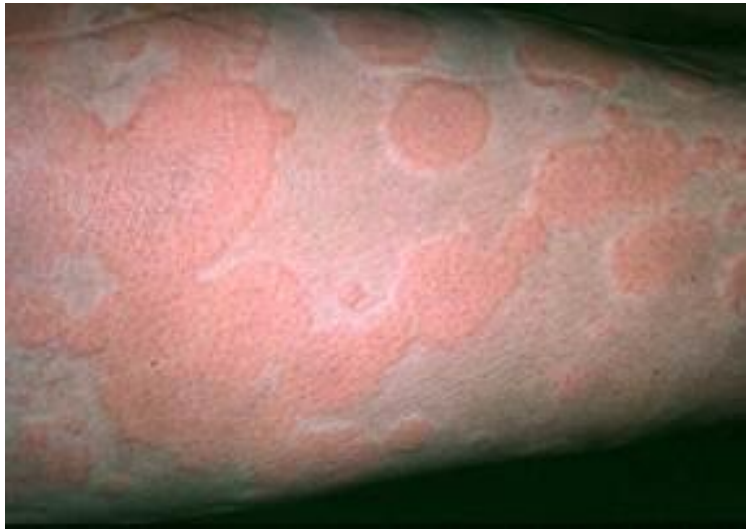


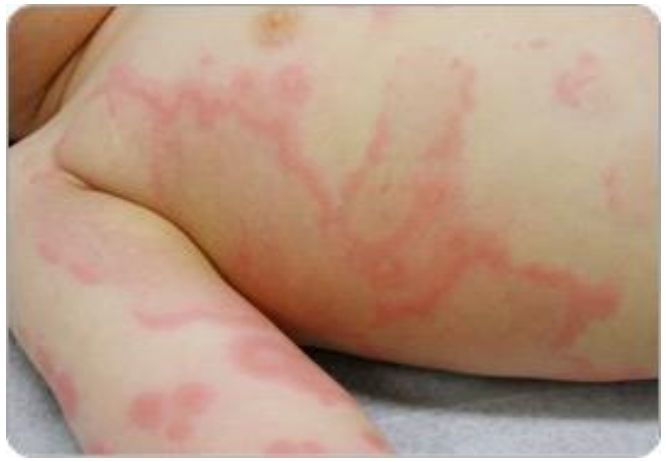
Delayed
Urticaria

## Viral exanthem

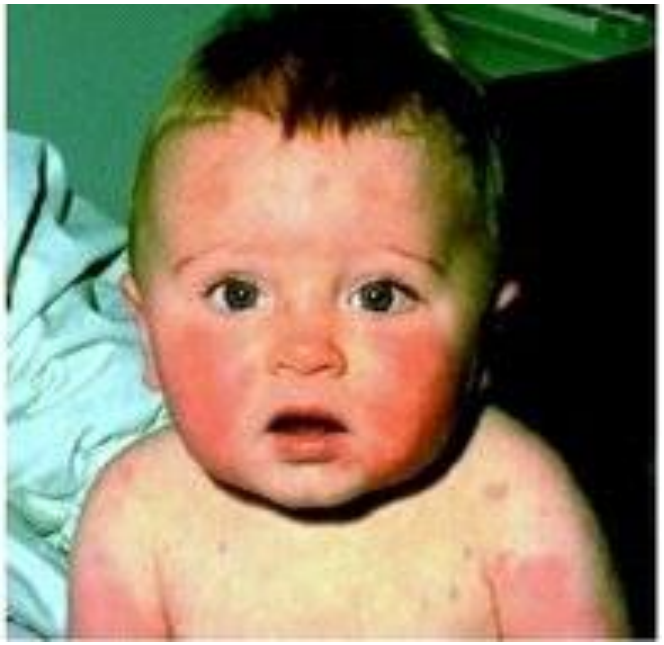


## Erythema Multiforme serpiginous, sometimes with central clearing





## Roseola



# WHAT CAN YOU DO TO DECREASE AMOXICILLIN/PENICILLIN ALLERGY LABELING AND IMPROVE PATIENT CARE?

1. Be SURE before labeling a patient amoxicillin allergic.

2. Remove allergy labels by obtaining good history.
   - Get more history.
   - Take pictures for RAVEN MMM.
   - Consult a pediatrician.

3. Perform an allergy trial.

# Introducing…

The Amoxicillin Allergy Trial Guideline!

Yukon-Kuskokwim HEALTH CORPORATION

Clinical Guidelines/Treatment Protocols • May 2019

# Amoxicillin Allergy Trials

## Background

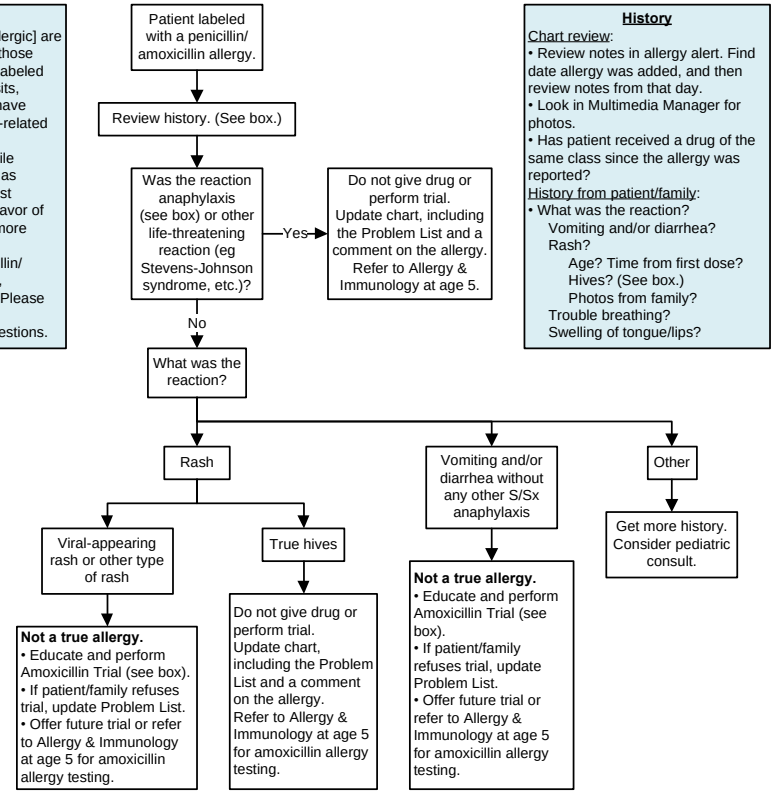
• Only 4-9% of those...labeled [penicillin-allergic] are currently allergic. It is important to identify those who are not allergic, because children mislabeled as penicillin-allergic have more medical visits, receive more antibiotic prescriptions, and have longer hospitalizations with more antibiotic-related complications.[1]
• Up to 10% of children develop rashes while receiving antibiotics. Most are diagnosed...as allergic to the implicated antibiotic, and most continue to avoid the suspect antibiotic in favor of alternatives, which may be less effective, more toxic, and more expensive.[2]
• Do not label a patient as allergic to penicillin/ amoxicillin unless he or she has true hives, anaphylaxis, or a life-threatening reaction. Please include photos of rashes in RAVEN.
• Please consult a pediatrician with any questions.

## Anaphylaxis

• Acute onset – several minutes to hours from exposure.
• Generalized hives, pruritis or flushing, swelling of lips/tongue/uvula, and at least one of the following:
  Dyspnea, bronchospasm, stridor
  Hypotension
  Evidence of hypoperfusion of end-organs
  Persistent crampy abdominal pain and/or vomiting

## Hives vs Viral Rash

• True hives are raised, itchy, larger than dime-sized, come and go, move around the body, and change shape and size.
• Keep in mind that many parents refer to any rash as "hives." Get a description every time.
• A viral exanthem is typically diffuse, fine, pinpoint red dots and can be dense, coalesced, larger raised lesions. The rash typically covers the face and chest but can cover the whole body. The rash typically worsens and takes days to clear.




## History

Chart review:
• Review notes in allergy alert. Find date allergy was added, and then review notes from that day.
• Look in Multimedia Manager for photos.
• Has patient received a drug of the same class since the allergy was reported?

History from patient/family:
• What was the reaction?
  Vomiting and/or diarrhea?
  Rash?
    Age? Time from first dose?
    Hives? (See box.)
    Photos from family?
  Trouble breathing?
  Swelling of tongue/lips?

## Amoxicillin Trial Procedure[2]

1. Obtain VS. Perform physical exam, including lung exam. Have appropriate dose of EpiPen or epinephrine available.
Epinephrine (1 mg/mL): 0.01 mg/kg (or 0.01 mL/kg) IM q5-15 minutes.
Per AAP recommendations:
  • 7.5-25 kg: use EpiPen Jr (0.15 mg)
  • ≥ 25 kg: use EpiPen (0.3 mg)
2. Calculate weight-based dose of amoxicillin. Give patient 10% of that dose.
3. Place patient in nearby room and instruct caregiver to notify staff of any changes in status.
4. If no reaction by 20 minutes, give patient remaining 90% of weight-based dose of amoxicillin.
5. Observe another 60 minutes. If no reaction, check VS and physical exam. If all stable, discharge home with regular course of drug.
6. Give patient and family amoxicillin trial education sheet.
7. Update allergy alert in RAVEN. Click the allergy in the banner. Right click over the drug name and choose "cancel." On the "reason" drop-down menu, choose "OK on Retrial."


**References**

1. Kelso JM. "Provocation challenges to evaluate amoxicillin allergy in children." JAMA Pediatrics 2016;170(6):e160282.
2. Mill C, et al. "Assessing the diagnostic properties of a graded oral provocation challenge for the diagnosis of immediate and nonimmediate reactions to amoxicillin in children." JAMA Pediatrics. 2016;170(6):e160033.


This guideline is designed for the general use of most patients but may need to be adapted to meet the special needs of a specific patient as determined by the medical practitioner.
Approved by MSEC 5/8/19.
**If comments about this guideline, please contact Jane_McClure@ykhc.org.**

# Here's where it is:

YKHC

- GENERAL INFORMATION
- NEW HIRE ORIENTATION
- EMERGENCY SERVICES
- PRIMARY CARE SERVICES
- HOSPITAL SERVICES
- VILLAGE HEALTH
- TELEHEALTH SERVICES
- SPECIALTY CARE SERVICES
- DIAGNOSTIC SERVICES
- RESIDENTS
- CLINICAL RESOURCES

Category | Discussion

## Category:YKHC Guidelines

Click the link below to open the pdf file directly

YKHC Clinical Guidelines

**Contents** [hide]


1 Emergency Department
- 1.1 Emergency Department Guidelines
- 1.2 Emergency Department Protocols

2 Pediatrics
- 2.1 Pediatric Emergency Guidelines
- 2.2 Pediatric Outpatient Guidelines
- 2.3 Pediatric Neonatal Guidelines
- 2.4 Pediatric Protocols/Reference

3 OB
- 3.1 OB Guidelines
- 3.2 OB Protocols

4 Outpatient
- 4.1 Outpatient Guidelines
- 4.2 Outpatient Protocols


## Pediatrics

### Pediatric Emergency Guidelines

*(For Pediatric Critical Care Weight-Based Guide, see Pediatric Critical Care Guide)*

- Critical Care and Medevac Guide – Pediatric
- Intubation – Pediatric
- High-Flow Nasal Cannula (HFNC) — Pediatric
- Sepsis – Pediatric
- Seizure Evaluation – Pediatric
- Seizure Treatment – Pediatric
- Fever – Infants 0-90 days
- Croup/Stridor: Evaluation & Treatment
- Bronchiolitis / Wheezing – 3-24 Months
- Pneumonia – Pediatric More Than 3 Months
- Suspected Child Sexual Abuse Procedure
- Head Injury / Concussion Under 18 Years
- Amoxicillin Allergy Trials

### Pediatric Outpatient Guidelines

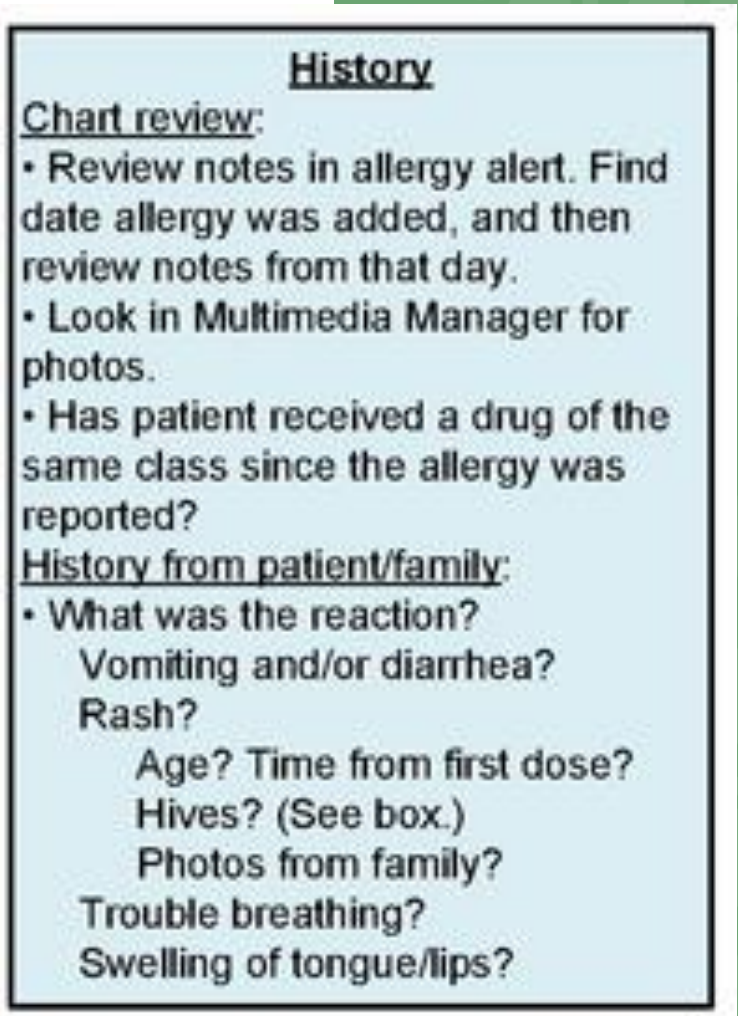
- UTI – Children 3 Months–5 Years
- Otitis Media 3 months–12 years
- Sinusitis More Than 5 Years
- Attention Deficit Hyperactivity Disorder in Children
- TB Evaluation & Treatment – Pediatric
- Seizure Evaluation – Pediatric
- Chronic Cough/Bronchiectasis – Pediatrics
- Lead Evaluation – Pediatrics
- Acute Cervical Lymphadenitis Evaluation & Treatment – Pediatrics
- Amoxicillin Allergy Trials

# Here’s what it says:

# STEP 1: Get more information

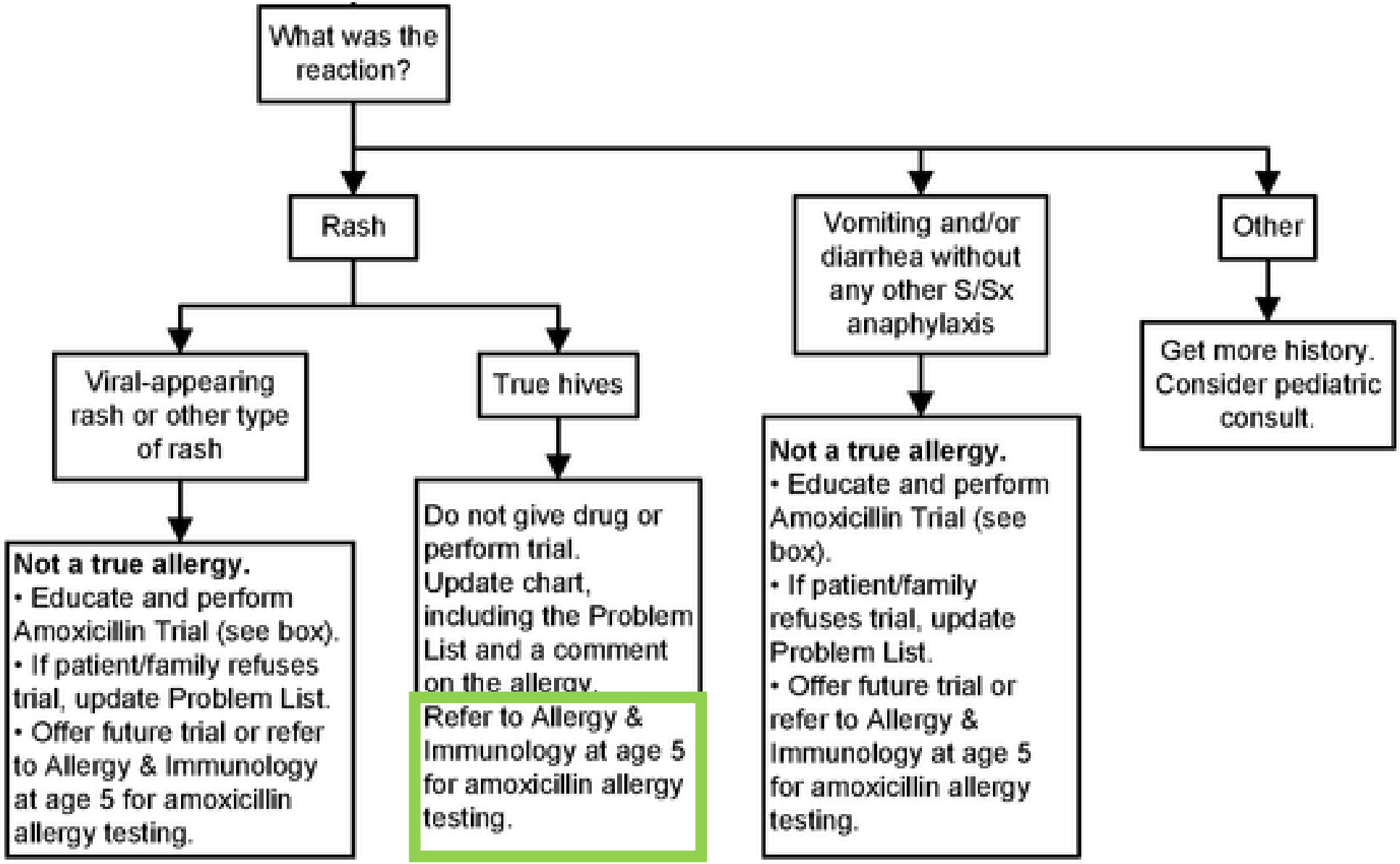
What type of reaction did the patient have?

1. Vomiting or diarrhea? (Definitely not an allergy)
2. Rash?
   - -At what age did the rash occur?
   - -Did the rash start right after taking the medicine or a number of days later?
   - -Are there any pictures or documentation of what the rash looked like?
   - -What did the rash look like? Many things are called hives – was the rash raised, itchy, bigger than dime size, moved around the body, and changed shape and size?
   - -**OR** was it a fine red rash all over the body that stayed for several days?
3. Swelling of the lips and/or trouble breathing?
4. Has the patient received any treatment with penicillin, amoxicillin, or Augmentin since he/she had the first reaction?



## STEP 2: Decide

# Was it likely to be a true allergy or not?


What was the reaction?
Rash
Viral-appearing rash or other type of rash
Not a true allergy.
• Educate and perform Amoxicillin Trial (see box).
• If patient/family refuses trial, update Problem List.
• Offer future trial or refer to Allergy & Immunology at age 5 for amoxicillin allergy testing.
True hives
Do not give drug or perform trial.
Update chart, including the Problem List and a comment on the allergy.
Refer to Allergy & Immunology at age 5 for amoxicillin allergy testing.
Vomiting and/or diarrhea without any other S/Sx anaphylaxis
Not a true allergy.
• Educate and perform Amoxicillin Trial (see box).
• If patient/family refuses trial, update Problem List.
• Offer future trial or refer to Allergy & Immunology at age 5 for amoxicillin allergy testing.
Other
Get more history. Consider pediatric consult.

# Update the Problem List:

1. No true allergy based on chart review and history:
   - Note if family wants allergy trial or not.
   - Note if allergy referral has been placed.
2. Possible allergy with not enough information on chart review.
   - Note if allergy referral has been placed.
3. Family history of allergy and family scared to let patient try the antibiotic despite education.
   - Note if allergy referral has been placed.

# EXAMPLE Diagnoses and Comments for Problem List

1. Amoxicillin Rash Diagnosis

Chart and history reviewed. No evidence of allergy to amoxicillin found. Family educated about the need to use appropriate, narrow spectrum antibiotics. *Patient has been scheduled for an Amoxicillin trial appt./ will consider an Amoxicillin trial appt. in the future OR refuses local Amoxicillin trial and has been referred for allergy testing/ will need referral for allergy testing at 5 years of age*.

2. Chart and history reviewed. Unable to determine if patient had a true allergic reaction to antibiotic. Family educated about the importance of using appropriate, narrow spectrum antibiotics if possible. *Patient has been referred for allergy testing/ will need referral for allergy testing at 5 years of age*.

3. Drug Allergy Family History (modify Drug Allergy problem).

Mother has penicillin allergy and does not want patient to receive amoxicillin. Family educated about lack of good research supporting genetic component of antibiotic allergies. *Amoxicillin Trial offered, but declined/patient referred (or will need referral at 5 years of age) to allergy and immunology for further testing.*

# STEP 3: If not a true allergy, do a trial

Give in a controlled environment and observe.

This can be done in clinics, ER, Fast Track, and inpatient settings.

Patient doesn’t need to be closely monitored. The waiting room is fine as long as the patient is close by.

Village Trials can be performed if health aides and family are on board. There is a wide range of acceptance. Some are enthusiastic, many are reluctant but willing to try after discussion. Some will not do it at all.

## Amoxicillin Trial Procedure[2]

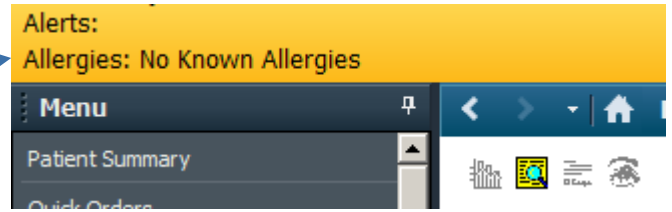
1. Obtain VS. Perform physical exam, including lung exam. Have appropriate dose of EpiPen or epinephrine available.
Epinephrine (1 mg/mL): 0.01 mg/kg (or 0.01 mL/kg) IM q5-15 minutes.
Per AAP recommendations:
    - 7.5-25 kg: use EpiPen Jr (0.15 mg)
    - ≥ 25 kg: use EpiPen (0.3 mg)
2. Calculate weight-based dose of amoxicillin. Give patient 10% of that dose.
3. Place patient in nearby room and instruct caregiver to notify staff of any changes in status.
4. If no reaction by 20 minutes, give patient remaining 90% of weight-based dose of amoxicillin.
5. Observe another 60 minutes. If no reaction, check VS and physical exam. If all stable, discharge home with regular course of drug.
6. Give patient and family amoxicillin trial education sheet.
7. Update allergy alert in RAVEN. Click the allergy in the banner. Right click over the drug name and choose "cancel." On the "reason" drop-down menu, choose "OK on Retrial."

# Step 4: The patient is not allergic!

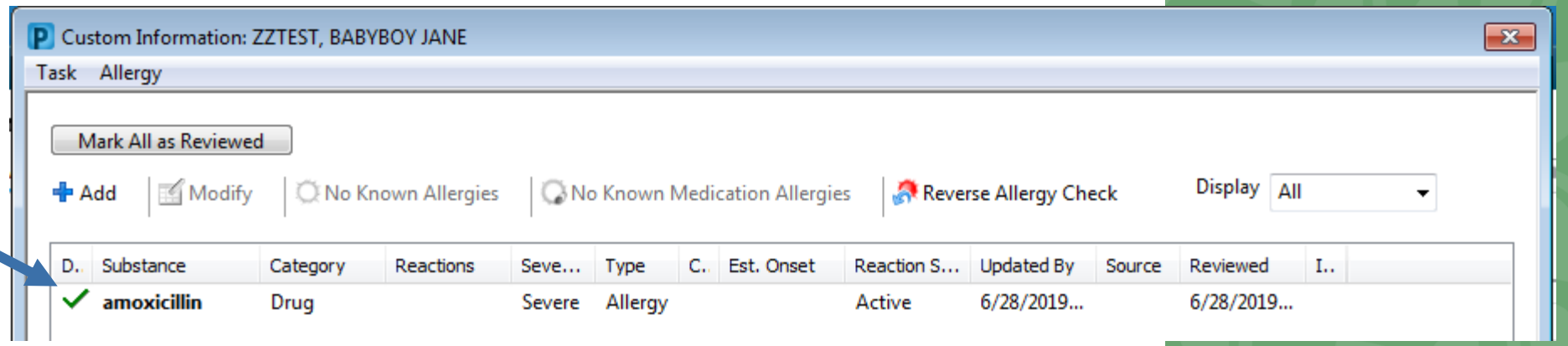
- Update the patient’s allergy on the RAVEN banner.

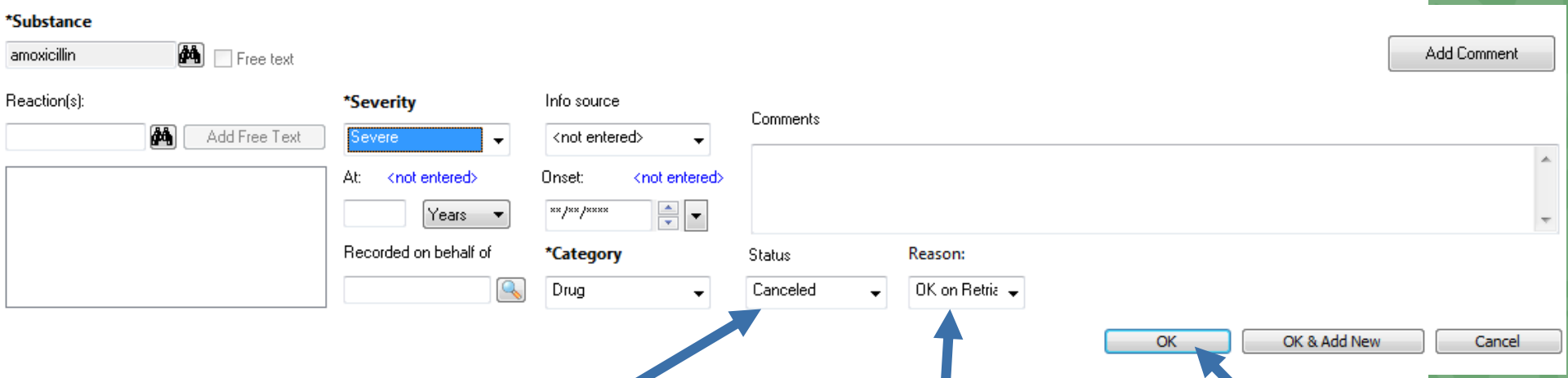
# How to change the allergy alert on the RAVEN banner

Click on Allergies.




Double click on the drug name.




Change the Status to “Canceled.”

Change the Reason to “OK on Retrial.”

Click OK.

# Patient Education Handout

- Go to…RAVEN→Patient Education: type in Amoxicillin Rash and click All

# ANTIBIOTIC RASHES

## WHAT IS AN ANTIBIOTIC RASH?

An amoxicillin, Augmentin, or penicillin rash is a non-allergic rash that occurs when a child is taking one of these medicines. The rash usually appears 2-5 days after the child starts taking the medicine, but may appear earlier or as late as the 16th day.
Symptoms of the rash include:

- Small (less than ¼ inch) widespread pink spots in a symmetrical pattern or slightly raised pink bumps.
- Small, flat, non-itchy spots.
- Appearing on one the chest, abdomen, or back and usually involving the face, arms, and legs.

## WHAT IS THE CAUSE?

Up to 10% of children taking amoxicillin, Augmentin, or penicillin get a non-allergic rash. These rashes are often caused by a viral infection such as Roseola. These are harmless rashes and do not mean that your child has an allergy to amoxicillin, Augmentin, or penicillin. An allergic reaction would cause hives (a different type of rash) or more severe symptoms.

## HOW LONG DOES IT LAST?

The rash usually lasts 3 days but can last up to 6 days.

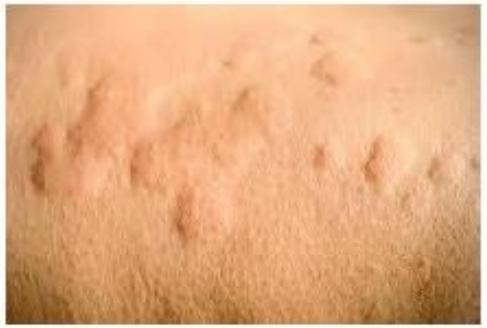
## HOW IS IT TREATED?

- No treatment is necessary, and the rash is not contagious
- Keep your child on the amoxicillin or other penicillin drug until the medicine is gone.
  - Stopping the medication can incorrectly label your child as allergic to the penicillin-family of antibiotics, which leads to other problems in the future.
  - A different antibiotic may not be necessary and could cause other problems.
- Stopping the medicine will not make the rash disappear any faster.
- Your child can take amoxicillin, Augmentin, or penicillin in the future when necessary. Only 5% of children get a rash again the next time.

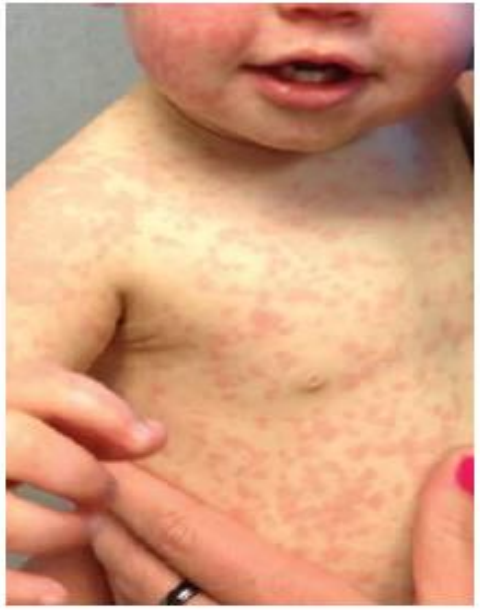
## WHEN SHOULD MY CHILD GET MEDICAL CARE?

- If the rash changes to hives, which are raised, itchy, and move around.
- If the rash becomes intensely itchy.
- If the rash becomes a lot worse or lasts more than 6 days.
- If your child has sudden onset of rash (within two hours of the first dose), any breathing or swallowing difficulty, or swelling of lips/face/tongue.
- If you have other concerns or questions.

HIVES



AMOXICILLIN RASH

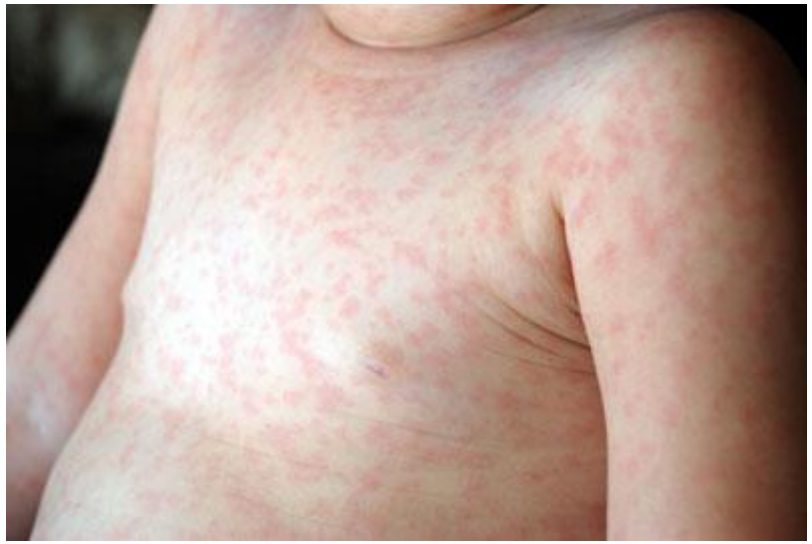


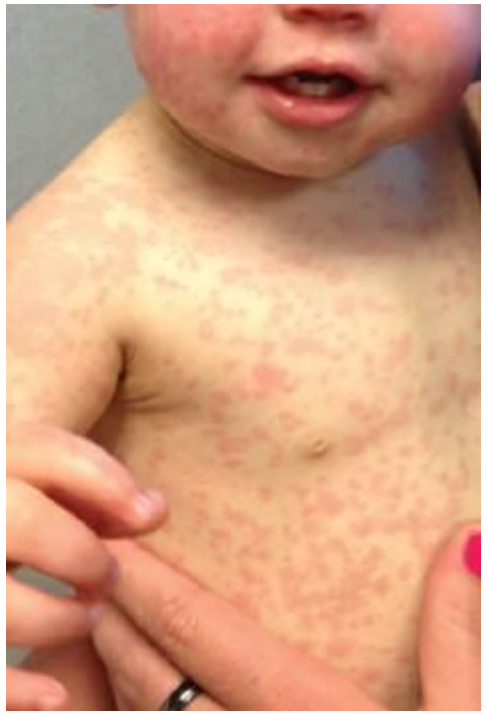
# Future Directions

- Stop incorrect amoxicillin (penicillin) allergy labeling.
- Chip away at the 3100 patients currently labeled with penicillin allergies.
- Ideas so far:
  1. Assign historical chart reviewers to whittle down the 3100 patients.
  2. Assign consultants to review chart prior to placing a penicillin allergy label (experienced gatekeeper).
  3. Make dedicated Amoxicillin Allergy Clinic time.
  4. Educate health aides, nurses, and providers about getting more history before adding a new allergy.
  5. ??

# Quick Rash Review

# Would you continue amoxicillin or give it again in the future?





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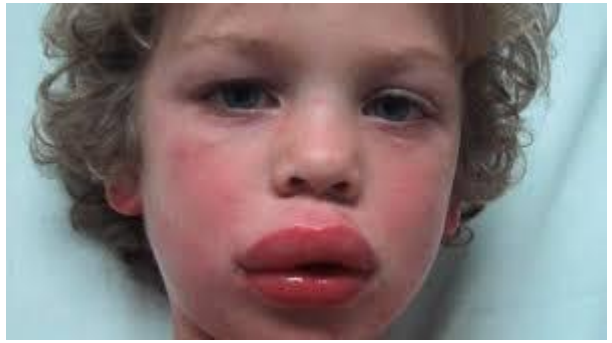

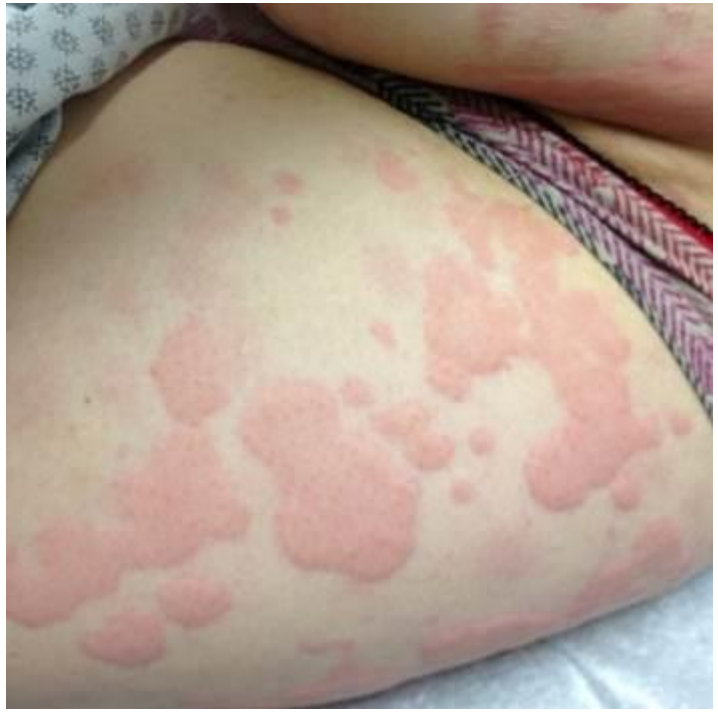

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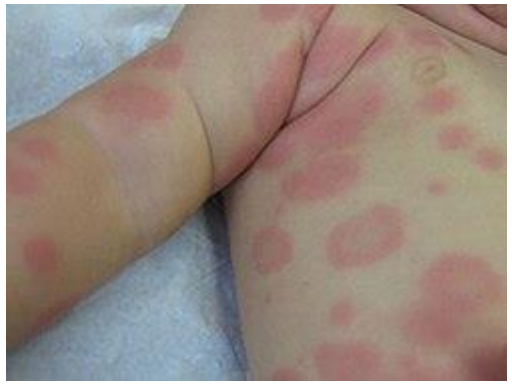

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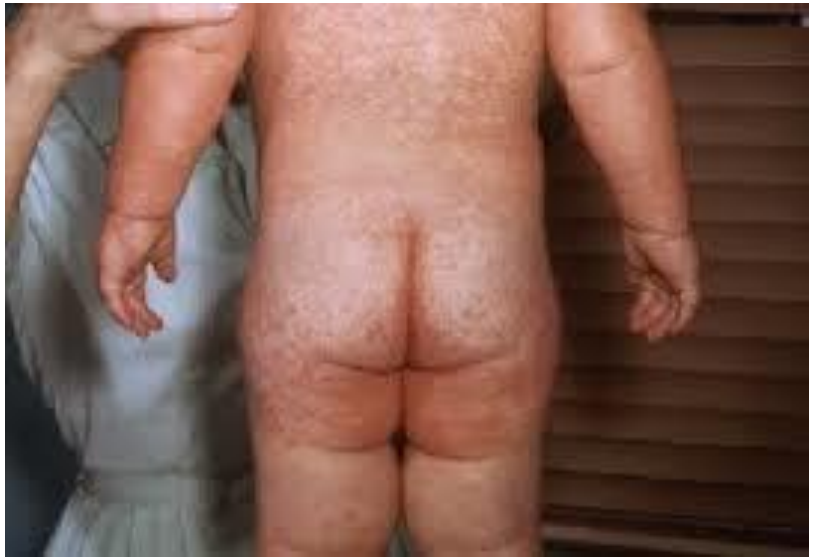

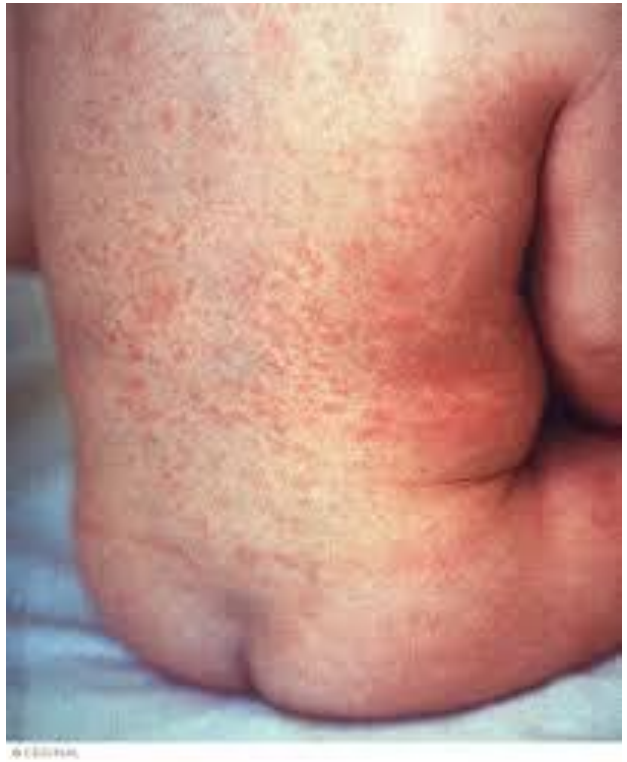

# Thank you!