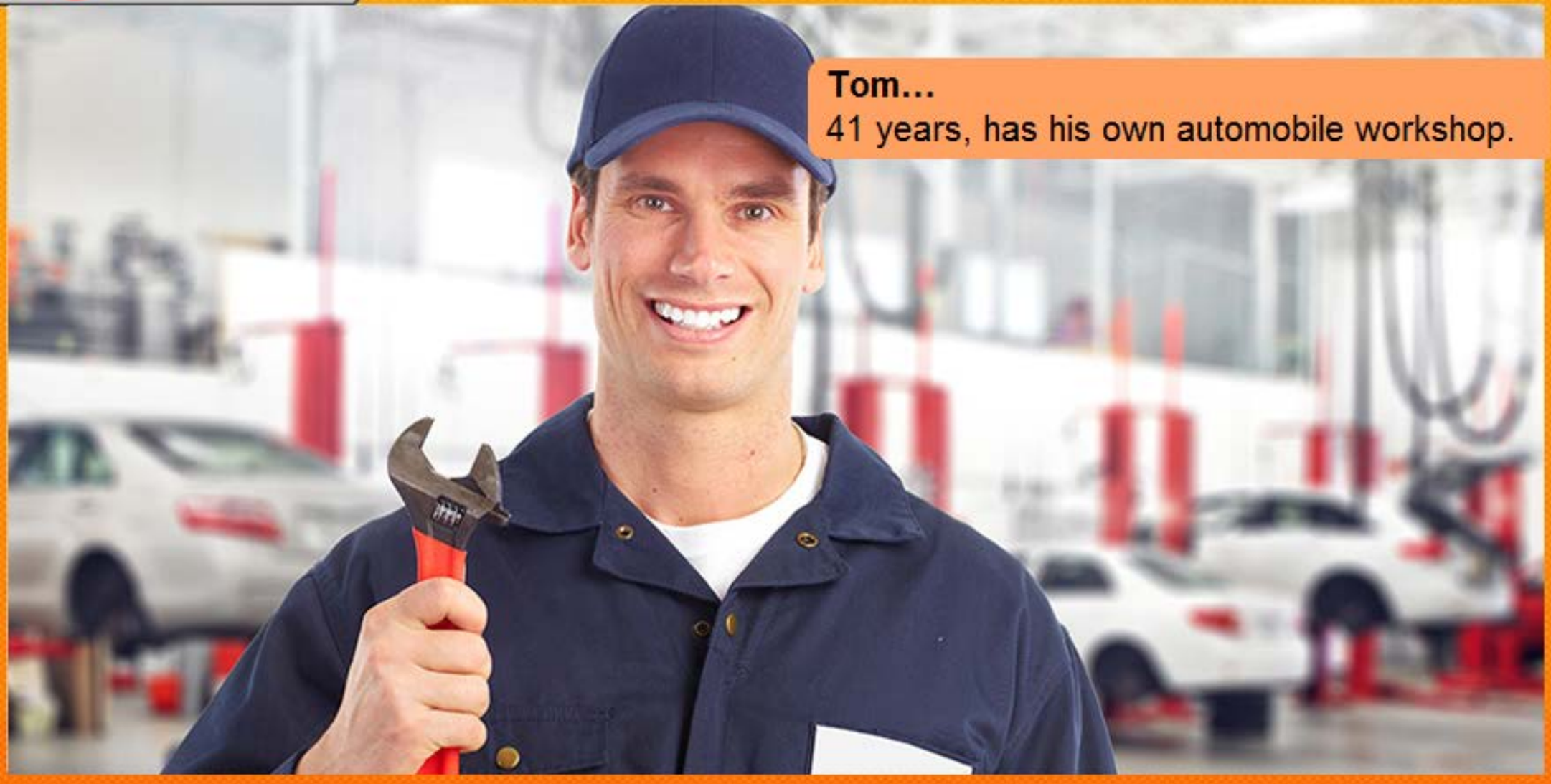
Augmentin® 875 mg Tablets

Amoxicillin as trihydrate 875 mg

Clavulanic Acid as potassium salt 125 mg

Zinc code: IL/CAM/0007/16.
Date of preparation: August 2016

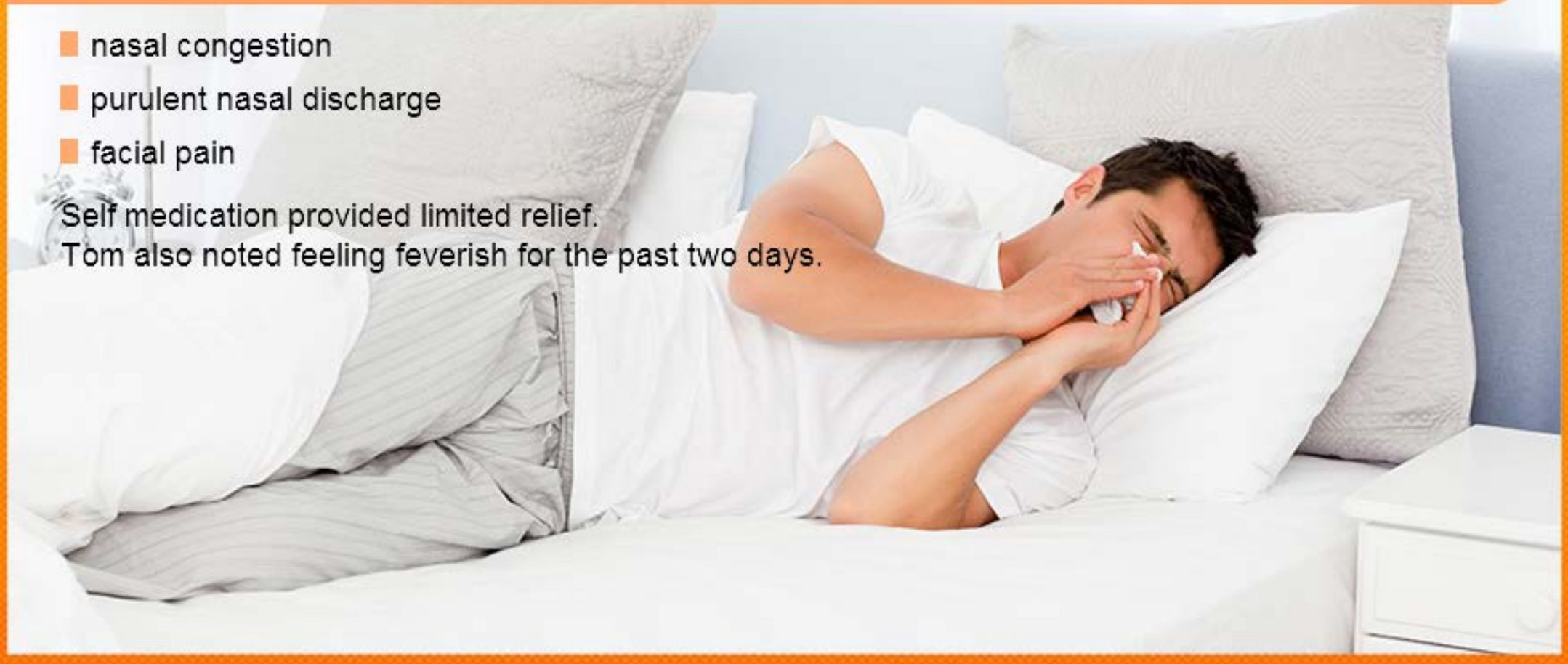
Disclaimer: This is an illustrative case study simulating real world experience



Since the past 10 days, Tom had the following symptoms that affected his routine activities:

- nasal congestion
- purulent nasal discharge
- facial pain

Self medication provided limited relief.
Tom also noted feeling feverish for the past two days.



Tom finally consulted his family physician.

Physical examination revealed:

- Fever (temperature 38.5°C)
- Facial tenderness on frontal area
- Nasal congestion

ENT examination revealed:

- Purulence in the nasal cavity
- Erythema of the nasal mucosa

Diagnosis:

Acute Bacterial RhinoSinusitis (ABRS)

Additional investigations

Imaging studies?

Radiographic confirmation of sinus disease for patients with uncomplicated ABRS is not necessary and is not advised.[1]

Imaging studies such as plain radiographs or CT are nonspecific and do not distinguish bacterial from viral rhinosinusitis.[1]

1. Chow A, Benninger M, Brook I, *et al* . IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112

Conventional criteria for diagnosis of sinusitis

Clinical criteria for diagnosis of ABRS

Conventional criteria for diagnosis of sinusitis

Of the physical findings the only finding shown to have diagnostic value is that of purulence in the nasal cavity or posterior pharynx.[1]

Conventional Criteria for the Diagnosis of Sinusitis Based on the Presence of at Least 2 Major or 1 Major and > 2 Minor Symptoms[2]

Major Symptoms	Minor Symptoms
• Purulent anterior nasal discharge	• Headache
• Purulent or discolored posterior nasal discharge	• Ear pain, pressure, or fullness
• Nasal congestion or obstruction	• Halitosis
• Facial congestion or fullness	• Dental pain
• Facial pain or pressure	• Cough
• Hyposmia or anosmia	• Fever (for subacute or chronic sinusitis)
• Fever (for acute sinusitis only)	• Fatigue

1. Rosenfeld R, Andes D , Bhattacharyya N, *et al* . Clinical practice guideline: Adult sinusitis Otolaryngology–Head and Neck Surgery (2007) 137, S1-S31.
2. Chow A, Benninger M, Brook I, *et al* . IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112

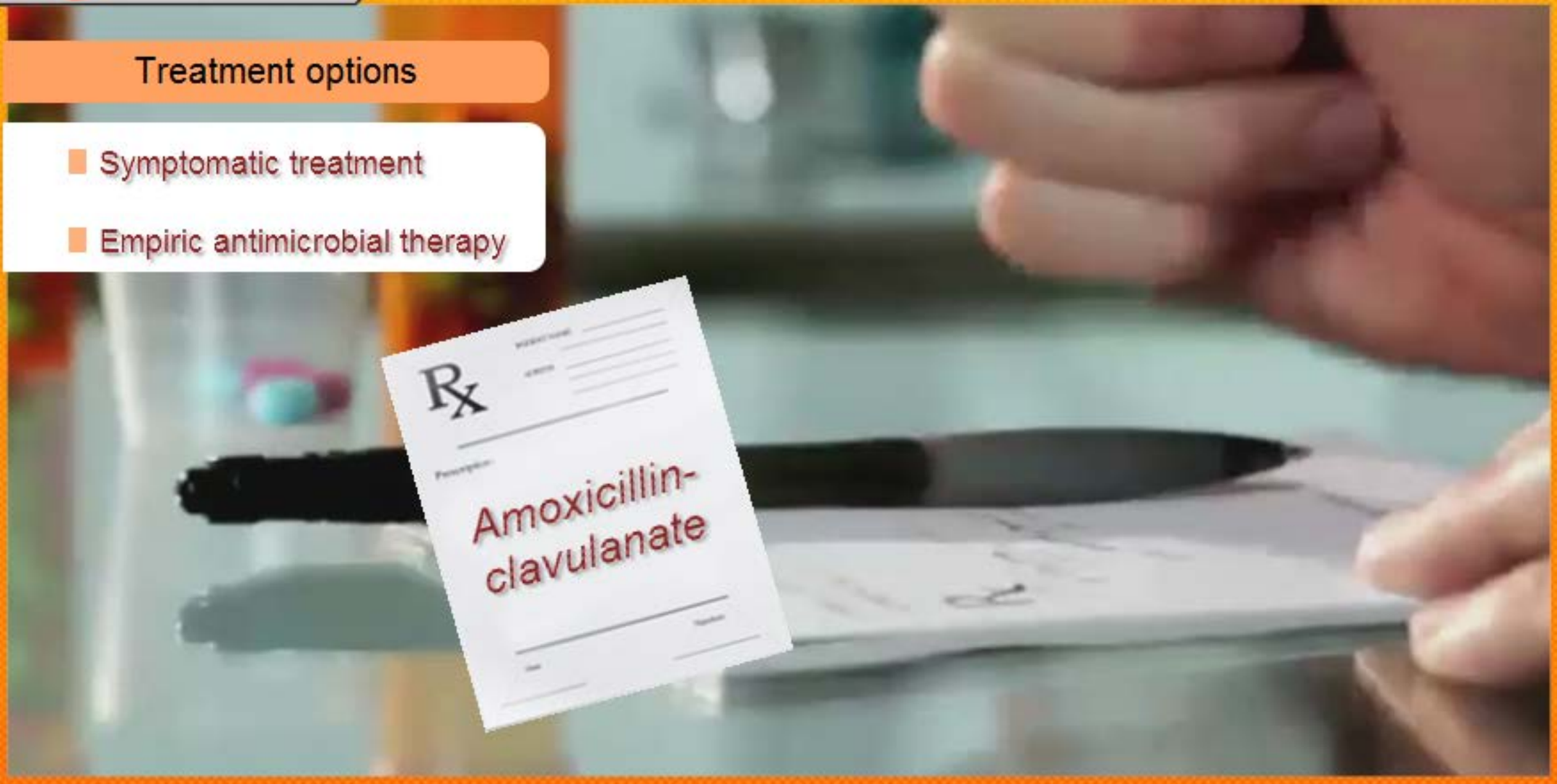
Three typical clinical presentations were emphasized to differentiate bacterial from viral rhinosinusitis[1]

- Onset with persistent symptoms that last ≥10 days and were not improving (This case)
- Onset with severe symptoms, characterized by high fever of at least 39°C (102°F) and purulent nasal discharge for at least 3–4 consecutive days at the beginning of illness; and
- Onset with worsening symptoms, characterized by typical viral URI symptoms that appear to improve followed by the sudden onset of worsening symptoms after 5–6 days (“double-sickening”)

1. Chow A, Benninger M, Brook I, *et al* . IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112

Treatment options

- Symptomatic treatment
- Empiric antimicrobial therapy



Treatment for symptomatic relief

Clinicians may prescribe symptomatic relief in managing ABRS.[1]

Pain relief is a major goal in managing ABRS.[1]

Neither topical nor oral decongestants and/or antihistamines are recommended as adjunctive treatment in patients with ABRS.[2]

1. Rosenfeld RM, Andes D, Bhattacharyya N, *et al* . Clinical practice guideline: adult sinusitis. Otolaryngol Head Neck Surg.2007 Sep; 137(3 Suppl):S1-31.
2. Chow A, Benninger M, Brook I, *et al* . IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112

Empiric antimicrobial therapy

A. A watchful waiting strategy is only reasonable if one is uncertain about the diagnosis of ABRS owing to mild symptoms but cannot be recommended when more stringent clinical criteria for the diagnosis of ABRS are applied.[1]

B. Prompt initiation of antimicrobial therapy should shorten the duration of illness, provide earlier symptomatic relief, restore quality of life, and prevent recurrence or suppurative complications.[1]

1. Chow A, Benninger M, Brook I, *et al* . IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112

Infectious Diseases Society of America

Guideline recommendation[1]

Amoxicillin-clavulanate recommended as:

First-line initial empirical antimicrobial therapy for acute bacterial rhinosinusitis in both adults and children

Also recommended as second line antimicrobial therapy for acute bacterial rhinosinusitis in both adults and children who experience treatment failure to other first-line agents

First-line dose: Amoxicillin-clavulanate (45 mg/kg/day PO bid) for children, amoxicillin-clavulanate (500 mg/125 mg PO tid, or 875 mg/ 125 mg PO bid) for adults

Second line dose: Amoxicillin-clavulanate (90 mg/kg/day PO bid) for children, amoxicillin-clavulanate (2000 mg/125 mg PO) for adults

1. Chow A, Benninger M, Brook I, *et al* . IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112

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Soon he was fit and spending quality time with his family.

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Achieves adequate concentration in sinus tissue[1,2]

Established clinical and bacteriological efficacy[3,4,5,6]

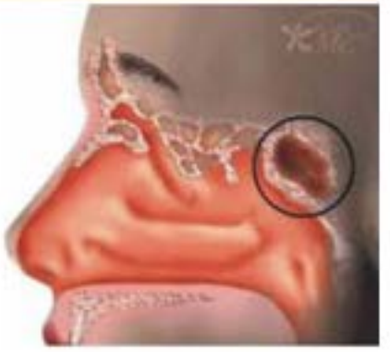
Guideline recommendation[8]

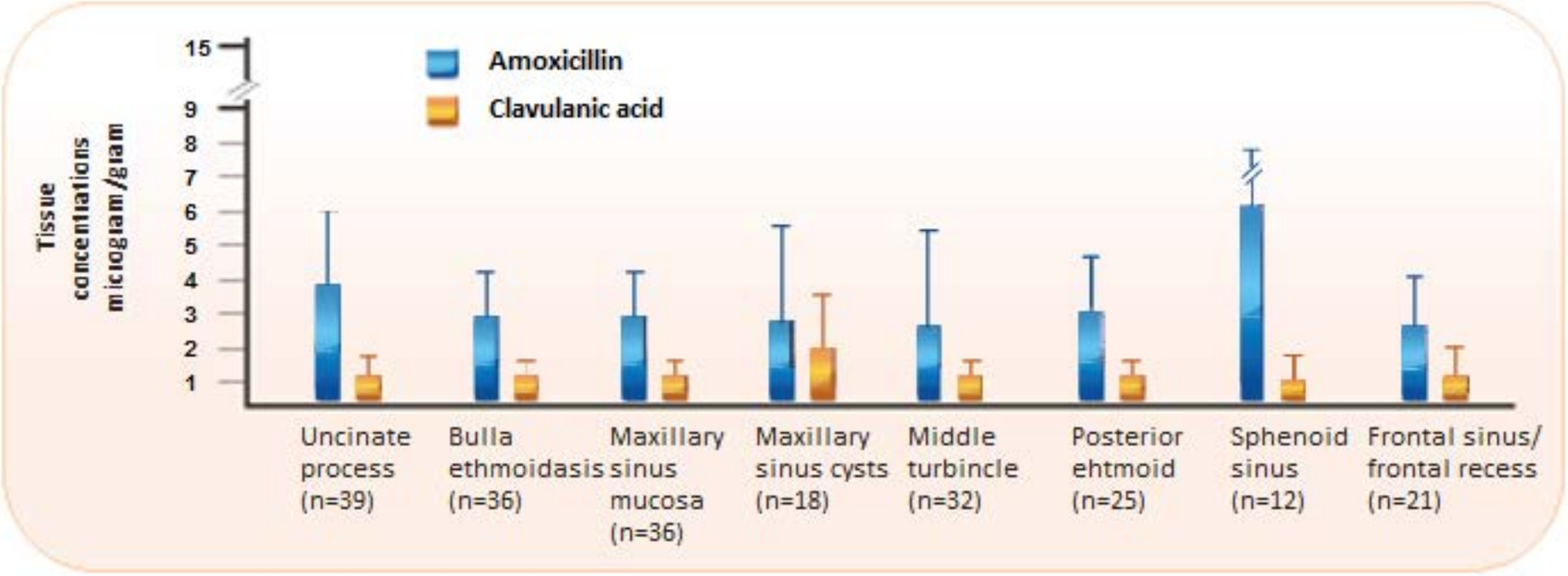
Clarithromycin | Dosage | Moxifloxacin

1. Dagan R, Klugman KP, Craig WA *et al*. Evidence to support the rationale that bacterial eradication in respiratory tract infection is an important aim of antimicrobial therapy. J Antimicrob Chemother.2001 Feb; 47(2):129-40.
2. Dinis PB, Monteiro MC, Martins ML *et al*. Sinus tissue pharmacokinetics after oral administration of amoxicillin/clavulanic acid. Laryngoscope.2000 Jun;110(6):1050-5.
3. Riffer E, Spiller J, Palmer R, *et al*. Once daily clarithromycin extended-release vs twice-daily amoxicillin/clavulanate in patients with acute bacterial sinusitis: a randomized, investigator-blinded study.
Curr Med Res Opin. 2005 Jan;21(1):61-70.
4. Arrieta JR, Galgano AS, Sakano E, *et al*. Moxifloxacin vs amoxicillin/clavulanate in the treatment of acute sinusitis.Am J Otolaryngol 2007 Mar-Apr; 28(2) :78-82.
5. Dagan R, Klugman KP, Craig WA *et al*. Evidence to support the rationale that bacterial eradication in respiratory tract infection is an important aim of antimicrobial therapy. J Antimicrob Chemother. 2001 Feb; 47(2):129-40.
6. Gwaltney JM Jr, Savolainen S, Rivas P, *et al*. Comparative effectiveness and safety of cefdinir and amoxicillin-clavulanate in treatment of acute community-acquired bacterial sinusitis. Cefdinir Sinusitis Study Group. Antimicrob Agents Chemother. 1997 Jul;41(7):1517-20.
7. Augmentin 875 PI MOH approved.
8. Chow A, Benninger M, Brook I, *et al*. IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults, Clin Infect Dis. 2012 Apr;54(8):e72-e112
Images and videos credit: www.shutterstock.com
*CARTI: community acquired respiratory tract infection
#: Susceptibility patterns may vary with time and geography, refer to local susceptibility data before prescribing

Augmentin in Sinusitis: adequate tissue concentration

- Antimicrobial therapy should eradicate bacteria from site of infection and minimize carriage[1]
- Amoxicillin displayed adequate tissue levels throughout the sinuses, high enough to cover common susceptible pathogens[2]





Adapted from reference 2

Fig: Overall mean concentrations and standard deviations of both amoxicillin & calvulanate at different sinonasal sites[2]

1. Dagan R, Klugman KP, Craig WA *et al* . Evidence to support the rationale that bacterial eradication in respiratory tract infection is an important aim of antimicrobial therapy. J Antimicrob Chemother.2001 Feb; 47(2):129-40.
2. Dinis PB, Monteiro MC, Martins ML *et al* . Sinus tissue pharmacokinetics after oral administration of amoxicillin/clavulanic acid. Laryngoscope.2000 Jun;110(6):1050-5.

Established clinical and bacteriological efficacy[1,2,3]

Year/Author	Augmentin dose	Comparator dose	Clinical efficacy	Bacteriological efficacy
Riffer E, *et al*. 2005	Amoxicillin/clavulanate 875mg/125mg twice daily for 14 days	Clarithromycin ER 1000mg once daily	98% clinical cure rate in clinically evaluable patients in the clarithromycin ER group and 97% in the amoxicillin/clavulanate group	94% pathogen eradication rates in the clarithromycin ER group and 98% in the amoxicillin/clavulanate group
Arrieta JR, *et al*. 2007	500/125mg 3 times daily for 10 days	Moxifloxacin 400mg once daily for 7 days	Clinical success rate • Moxifloxacin: 93.4% • Amoxicillin/clavulanate: 92.7%	Documented bacteriological eradication plus presumed eradication rates • Moxifloxacin: 96.5% • Amoxicillin/clavulanate: 96.7%
Dagan R, *et al*. 2001	-	-	-	Documented efficacious reduction in nasopharyngeal carriage of penicillin-susceptible & resistant *S. pneumoniae* as compared to cefixime

1. Riffer E, Spiller J, Palmer R, *et al* . Once daily clarithromycin extended-release vs twice-daily amoxicillin/clavulanate in patients with acute bacterial sinusitis: a randomized, investigator-blinded study. Curr Med Res Opin. 2005 Jan;21(1):61-70.
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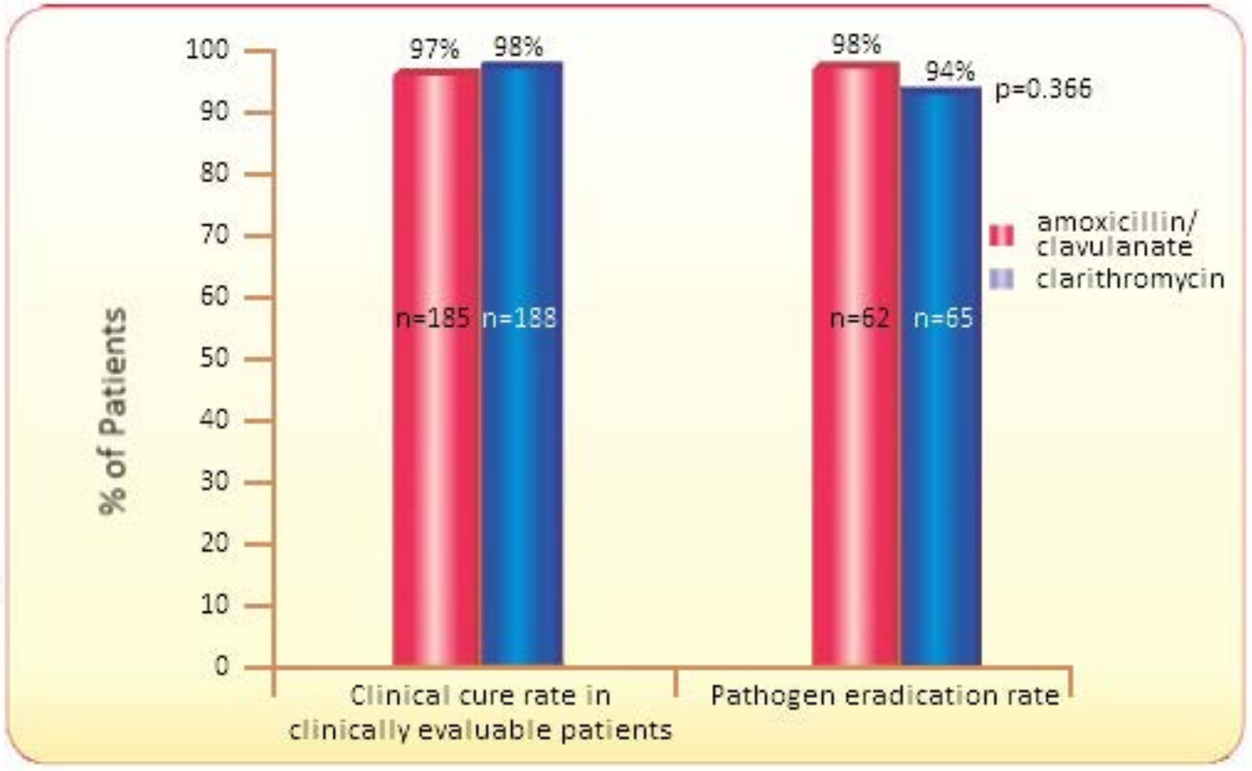
Amoxicillin-clavulanate vs. Clarithromycin[1]

- 98% clinical cure rate in clinically evaluable patients in the clarithromycin ER group and 97% in the amoxicillin/clavulanate group 95% CI for the difference in cure rates [–2.4%, 4.7%]
- 94% pathogen eradication rates in the clarithromycin ER group and 98% in the amoxicillin/clavulanate group 95% CI for the difference in eradication rates [–12.0%, 2.9%]



In a controlled, multicenter, investigator-blinded study, 437 ambulatory patients at least 12 years old with signs/symptoms and radiographic findings of acute sinusitis were randomized to receive clarithromycin extended release (ER)1000 mg once daily or amoxicillin/ clavulanate 875 mg/l25 mg twice daily for 14 days.

Clinical and bacteriological response comparable to clarithromycin ER in acute bacterial sinusitis patients

1. Riffer E, Spiller J, Palmer R *et al* . Once daily clarithromycin extended-release vs twice-daily amoxicillin/clavulanate in patients with acute bacterial sinusitis: a randomized, investigator-blinded study. Curr Med Res Opin.2005 Jan;21(1):61-70.

Augmentin 875 Indication[1]

Augmentin 875 mg Tablets Indication:

Augmentin is indicated for the treatment of the following infections in adults and children:

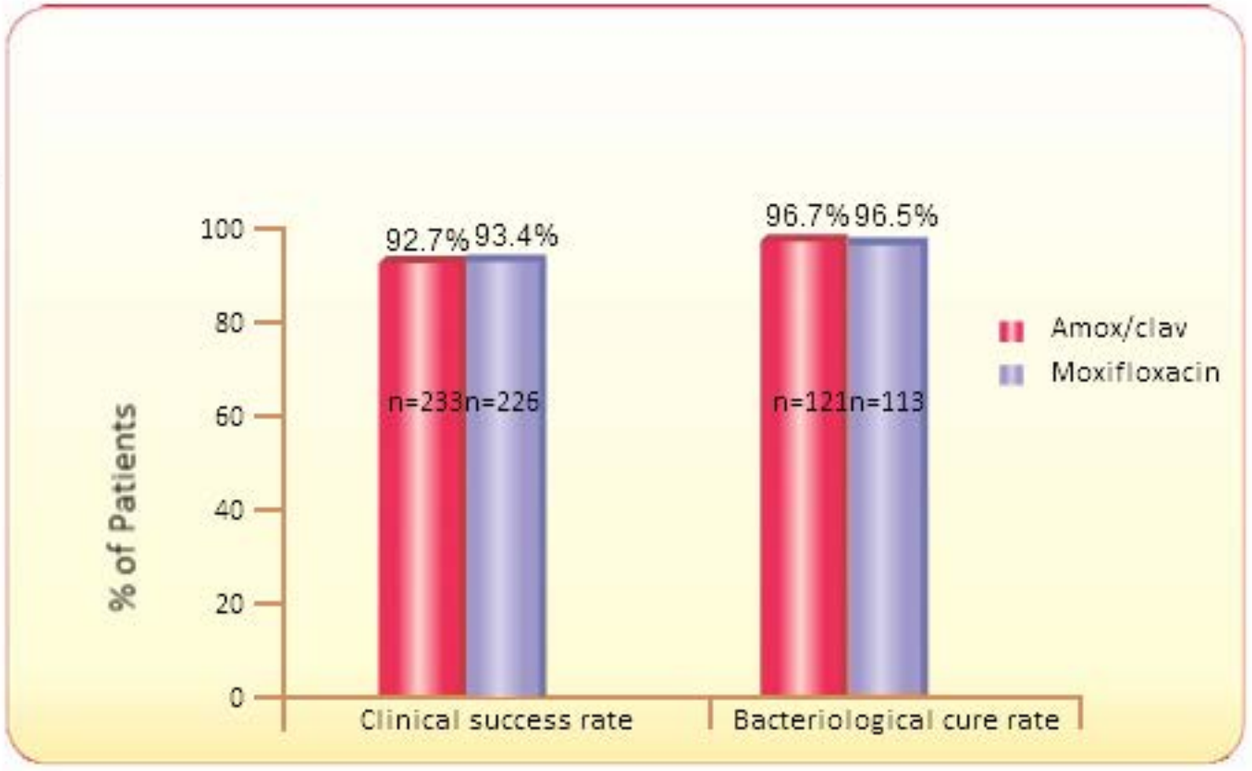
- Acute bacterial sinusitis (adequately diagnosed)
- Acute otitis media
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Cystitis
- Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

1. Augmentin PI MOH approved

Amoxicillin-clavulanate vs. Moxifloxacin[1]

- Similar clinical success rate (93.4%) in the moxifloxacin group to that in the amoxicillin/clavulanate group (92.7%) at test-of-cure visit (95% CI, -3.93% to 5.36%)
- Similar documented bacteriological eradication plus presumed eradication rates in the moxifloxacin (96.5%) and the amoxicillin/clavulanate (96.7%) (95% CI, -3.30% to 7.49%).



Five hundred seventy-five patients from Latin American countries were randomized to receive oral moxifloxacin 400 mg once daily for 7 days, or oral amoxicillin/clavulanate 500/125 mg 3 times daily for 10 days, in a prospective, open study

Clinical and bacteriological response equivalent to moxifloxacin in acute bacterial sinusitis patients

1. Arrieta JR, Galgano AS, Sakano E, *et al* . Moxifloxacin vs amoxicillin/clavulanate in the treatment of acute sinusitis. Am J Otolaryngol. 2007 Mar-Apr;28(2):78-82.

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MAIN SAFETY DATA

- Well established safety profile following many years of clinical usage in the treatment of bacterial infections
- Contraindicated in patients with known hypersensitivity to beta-lactam antibiotics (penicillins and cephalosporins). Before initiating therapy with amoxicillin-clavulanate, careful enquiry should be made concerning previous hypersensitivity reactions to antibiotics.
- The most commonly reported adverse drug reactions are diarrhoea, nausea and vomiting. Nausea is more often associated with higher oral doses. If gastrointestinal reactions are evident, they may be reduced by taking Augmentin at the start of a meal.

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MAIN SAFETY DATA

- Antibiotic-associated colitis has been reported with nearly all antibacterial agents including amoxicillin and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients with diarrhoea during or after any antibiotic. Should antibiotic-associated colitis occur, Augmentin should immediately be discontinued, a physician be consulted and an appropriate therapy initiated.
- Prolonged use may result in overgrowth of Candida and other non-susceptible organisms
- Should be used with caution in patients with evidence of hepatic impairment. Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children. Signs and

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MAIN SAFETY DATA

- Should be used with caution in patients with evidence of hepatic impairment. Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children. Signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects

- Should be avoided in patients known or suspected to be suffering from infectious mononucleosis as use of the amoxicillin component has been associated with the occurrence of a morbilliform rash

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- Should be avoided in patients known or suspected to be suffering from infectious mononucleosis as use of the amoxicillin component has been associated with the occurrence of a morbilliform rash
- In patients with renal impairment the dosage may need to be adjusted
- Consideration should be given to local susceptibility data (where available) and official guidance on the appropriate use of antibacterial agents

1. Augmentin PI MOH approved.

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Medical information service: il.medinfo@gsk.com
Adverse events reporting service: il.safety@gsk.com , Tel: 03-9297100

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הינך מוזמן להיכנס לאתר

IL/CAM/0007/16
Date of preparation: August 2016

ל-PI המלא נא ללחוץ כאן

References

1. Dagan R, Klugman KP, Craig WA *et al*. Evidence to support the rationale that bacterial eradication in respiratory tract infection is an important aim of antimicrobial therapy.
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2. Dinis PB, Monteiro MC, Martins ML *et al*. Sinus tissue pharmacokinetics after oral administration of amoxicillin/clavulanic acid. Laryngoscope.2000 Jun;110(6):1050-5.

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