WHAT COULD BE DONE BY PRIMARY CARE DOCTORS?

Challenges & Opportunities for Antibiotic Stewardship Program
Symposium on Advanced Infection Control 2020
19-20 November 2020

DR LEO LUI
MBBS(HK), MRCP(UK), FRCPath, FHKCPath, FHKAM(Pathology),
MPH(CUHK), PDipID(HK), PDipMDPath(HK)
ICB, CHP / IDCTC, HAHO

GLOBAL IMPACT OF AMR

A worldwide problem

- Killing people 700,000 each year

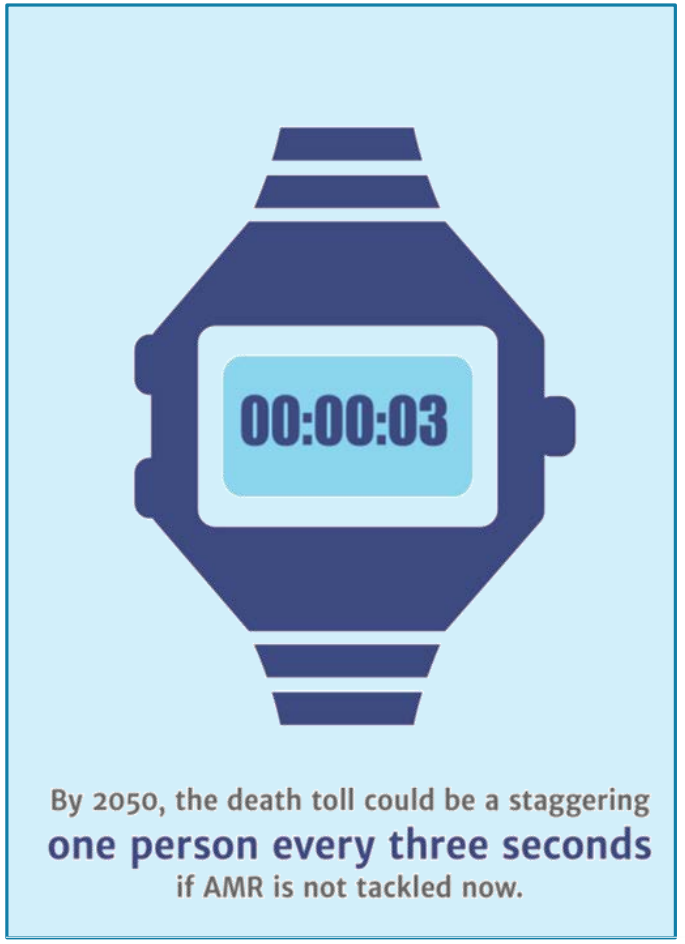
Potentially making medical procedures risky

- Cancer treatment, Joint replacement

By 2050

10 million people dying every year

100 trillion USD decrease in GDP

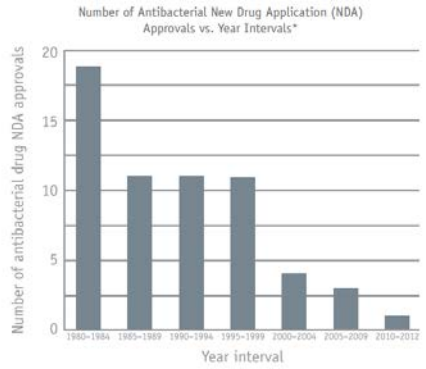


O'Neill, J. , 2016& WHO,2016

ANTIBIOTIC RESISTANCE INDENTIFIED		ANTIBIOTIC INTRODUCED	
penicillin-R *Staphylococcus*	1940		
		1943	penicillin
		1950	tetracycline
		1953	erythromycin
tetracycline-R *Shigella*	1959		
		1960	methicillin
methicillin-R *Staphylococcus*	1962		
penicillin-R pneumococcus	1965		
		1967	gentamicin
erythromycin-R *Streptococcus*	1968		
		1972	vancomycin
gentamicin-R *Enterococcus*	1979		
		1985	imipenem and ceftazidime
ceftazidime-R Enterobacteriaceae	1987		
vancomycin-R *Enterococcus*	1988		
levofloxacin-R pneumococcus	1996	1996	levofloxacin
imipenem-R Enterobacteriaceae	1998		
XDR tuberculosis	2000	2000	linezolid
linezolid-R *Staphylococcus*	2001		
vancomycin-R *Staphylococcus*	2002		
PDR-*Acinetobacter and Pseudomonas*	2004/5	2003	daptomycin
ceftriaxone-R *Neisseria gonorrhoeae* PDR-Enterobacteriaceae	2009	2010	ceftaroline
ceftaroline-R *Staphylococcus*	2011		

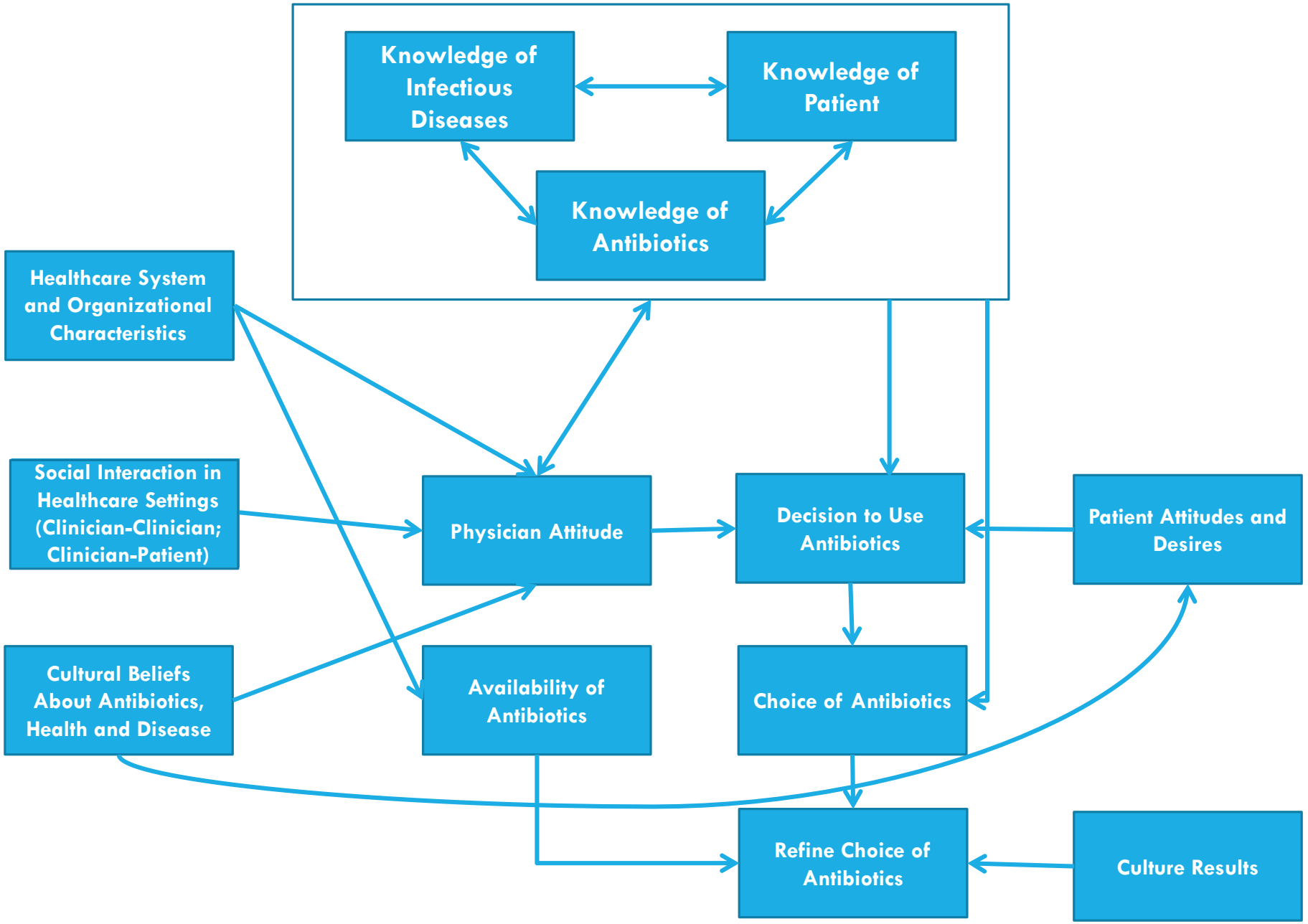
Tomorrow's Antibiotics: The Drug Pipeline

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.




More appropriate
use of antibiotics
Development of
new antibiotics
SLOW
SAFETY
FIRST
CAUTION

Conceptual Framework for Antibiotic Use



Tamar F. Barlam, et al. *Practical Implementation of an Antibiotic Stewardship Program*. Cambridge University Press. 2018

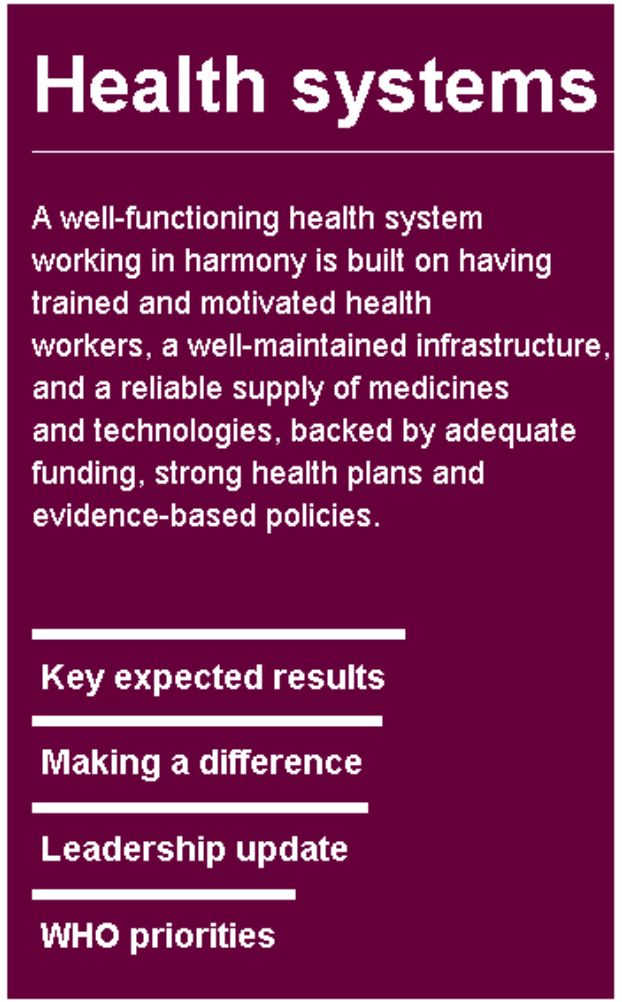
Stewardship is the careful and responsible management of resources to maximize the well-being of the population (Shiver, John Cantiello)

Health systems

Stewardship

Stewardship, sometimes more narrowly defined as governance, refers to the wide range of functions carried out by governments as they seek to achieve national health policy objectives. In addition to improving overall levels of population health, objectives are likely to be framed in terms of equity, coverage, access, quality, and patients' rights. National policy may also define the relative roles and responsibilities of the public, private and voluntary sectors - as well as civil society - in the provision and financing of health care.

Stewardship is a political process that involves balancing competing influences and demands. It will include: maintaining the strategic direction of policy development and implementation; detecting and correcting undesirable trends and distortions; articulating the case for health in national development; regulating the behaviour of a wide range of actors - from health care financiers to health care providers; and establishing effective accountability mechanisms. Beyond the formal health system stewardship means ensuring that other areas of government policy and legislation promote - or at least do not undermine - peoples' health. In countries that receive significant amounts of development assistance, stewardship will be concerned with managing these resources in ways that promote national leadership, contribute to the achievement of agreed policy goals, and strengthen national management systems. While the scope for exercising stewardship functions is greatest at the national level, the concept can also cover the steering role of regional and local authorities.



https://www.who.int/healthsystems/stewardship/en/ (accessed 19/6/2019)

ANTIBIOTIC STEWARDSHIP PROGRAMME (ASP)

"coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of the optimal antibiotic regimen including dosing, duration of therapy, and route of administration"

- Infectious Disease Society of America

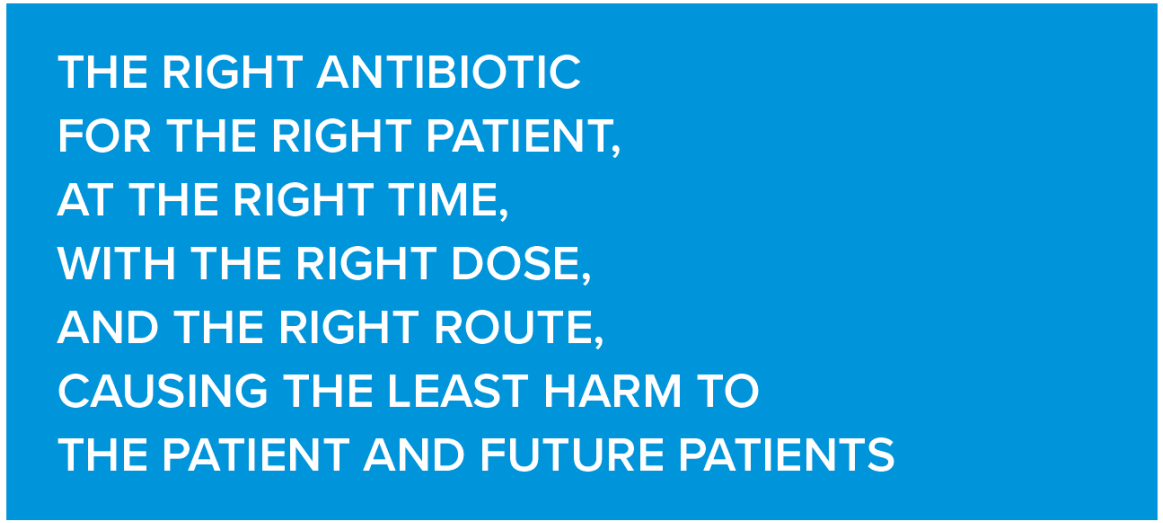


FIGURE 11
Adapted from http://www.cdc.gov/getsmart/healthcare/inpatient-stewardship

ANTIMICROBIAL STEWARDSHIP From Principles to Practice, BSAC

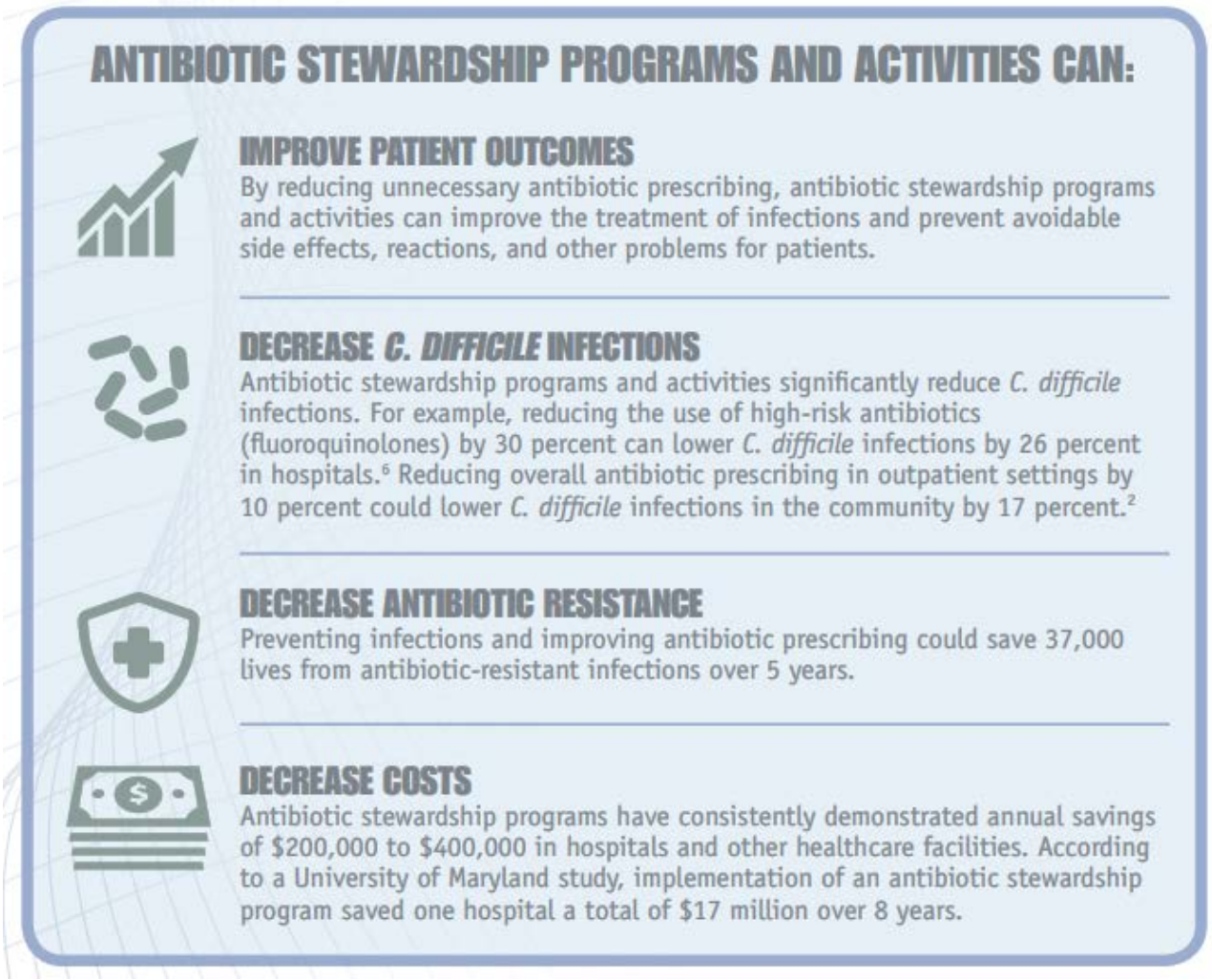
Do I need a new car in the first place ?

Is the car too powerful for my need?

Am I getting the right kind of car?

Am I staying on the road longer than necessary?

BENEFITS OF ASP



Primary Objectives

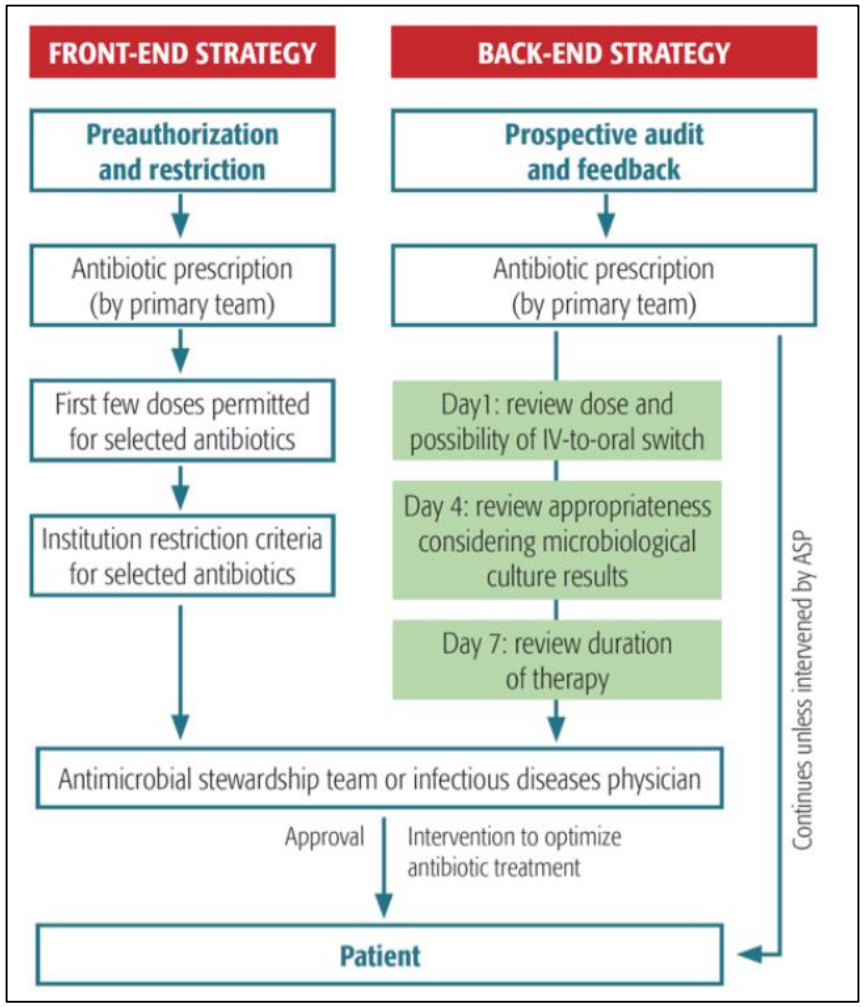
US CDC

HOW IS ASP DELIVERED?

Front-end	Pre-authorisation	• Restricted use of certain antibiotics requiring prior approval by ASP team or satisfying specific criteria on antibiotic order form
Back-end	Prospective audit and feedback	• ASP team review cases as clinical consultation • Take into account of culture & susceptibility results available in several days
adjunctive	Administrative Control	• Select antibiotics in hospital formulary • Differential reporting of antibiotic susceptibility results by laboratory
	Guidelines & educational activities	• Written protocols for infective syndromes • Cue cards for point-of-care use • Staff forums and regular sharings with clinicians
	Review and surveillance	• Antibiotic usage monitoring • Microbial resistance patterns & trends • Adverse effect rates e.g. C. *difficile* infections

Adapted from IMPACT 5th edition

FRONT-END & BACK-END



ANTIMICROBIAL STEWARDSHIP From Principles to Practice, BSAC

Pre-authorisation	Prospective or concurrent feedback
Advantages	
Prevents inappropriate initiation of antibiotics	Make ASP efforts more visible
Prompts review of clinical parameters before initiating therapy	Frequency of recommendation can be more flexible
Facilitates a rapid response to antibiotic shortage	Provide educational benefits to clinicians
Direct control over antibiotic use	Address de-escalation and duration
Disadvantages	
Effect mostly on empirical therapy	Compliance voluntary
Impact use on restricted agents only	More labor-intensive
Potential to manipulate system	Success is more operator-dependent
May delay initiation of therapy	Take longer to achieve use reduction

Barlam TF, et al. Clin Infect Dis. 2016 May 15;62(10):e51-77

STAKEHOLDERS OF ASP

Surveillance

Hospital Director

IT support

Management & Administration

Microbiologists
ID physicians
IC nurses
ID Pharmacists

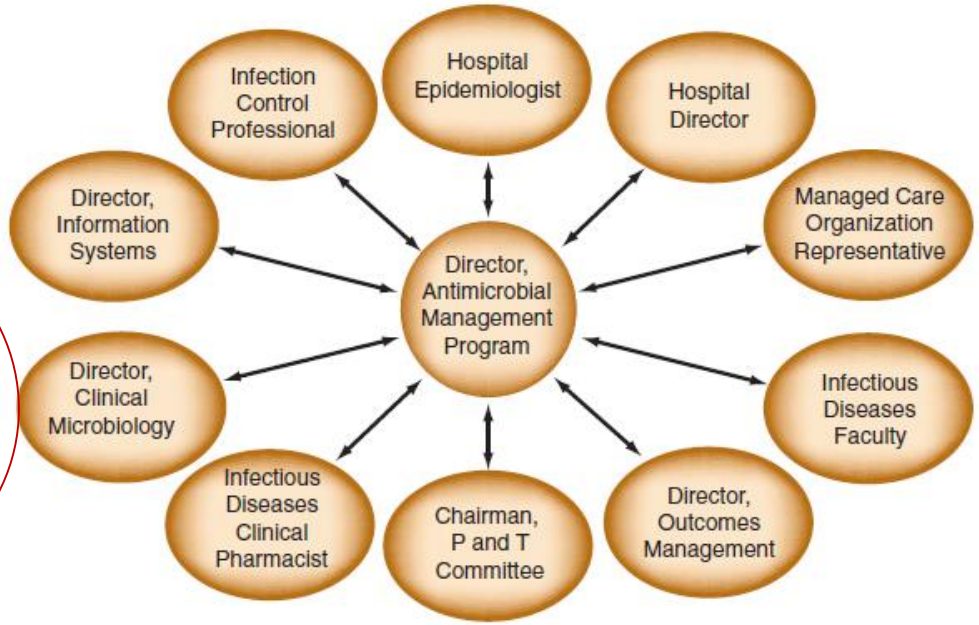


Figure 46-1 **Organizational structure of a comprehensive antimicrobial management program.** P and T, pharmacy and therapeutics. *(Adapted from John JF Jr, Fishman NO. Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospitals.* Clin Infect Dis. *1997;24:471.)*

Laboratory (diagnosis & antibiogram)

'Antibiotic Stewardship Team'

Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th Edition

Public Health Ontario | Santé publique Ontario
PARTNERS FOR HEALTH | PARTENAIRES POUR LA SANTÉ

Metrics Options

Consumption Metrics	Key Advantages	Key Disadvantages
Expenditures	-Purchase data easy to obtain -Easily understood by administrators	-Purchase data least accurate -Affected by changes in costs, formulary
Grams	-Purchase data easy to obtain -Not affected by price changes -Can be used to calculate DDD	-Purchase data least accurate
Defined Daily Doses (DDD)	-Easy to obtain -Benchmark between hospitals, regions, countries	-DDD values (WHO defined*) may not reflect typical doses and may change over time -Affected by formulary composition -Accuracy in pediatric, renal populations
Days Of Therapy (DOT)	-More accurate than DDD -Recommended by CDC**, NHSN** and Canadian Delphi Panel***	-Difficult to obtain -Favours those who use broad spectrum monotherapy -Accuracy in renal population
Length of Therapy (LOT)	-Most reflective of treatment duration -DOT/LOT proxy for combination versus monotherapy	-Cannot be used to compare use of specific drugs

* World Health Organization (see references)

** Centers for Disease Control and Prevention, US National Healthcare Safety Network

*** Morris AM, et al. Infect Control Hosp Epidemiol 2012;33:500

ANTIBIOGRAMS

Table PHLSB. Antibiogram for common Bacterial isolates from outpatient settings, PHLSB, 2018

Resistance of common bacterial isolates from outpatient setting, PHLSB, 2018															
	% resistant														
Organism	Specimen source	No. of isolates tested	Ampicillin	Amoxycillin-clavulanate	Ciprofloxacin	Clindamycin	Cotrimoxazole	Erythromycin	Gentamicin	Oxacillin	Penicillin	Levofloxacin	Nalidixic acid	Nitrofurantoin	ESBL +ve
Staphylococcus aureus	a	850				23		29	11	24					
MSSA	a	648				15		22	7	0					
MRSA	a	202				46		53	22	100					
Streptococcus pneumoniae	c	189						78			21[#]				
Streptococcus pyogenes	b	47						38			0				
Haemophilus influenzae	c	1849	47	15											
Escherichia coli	e	6373	68	6			37					31	73	1	17
Klebsiella pneumoniae	e	1147	100	7			18					6	20	15	9
Proteus mirabilis	e	709	38	12			35					18	45	100	
Campylobacter spp.	d	28						36							
Salmonella spp.	d	94	49		2[†]		20								

Specimen source: a, soft tissue; b, throat; c, sputum; d, enteric; e, urine.

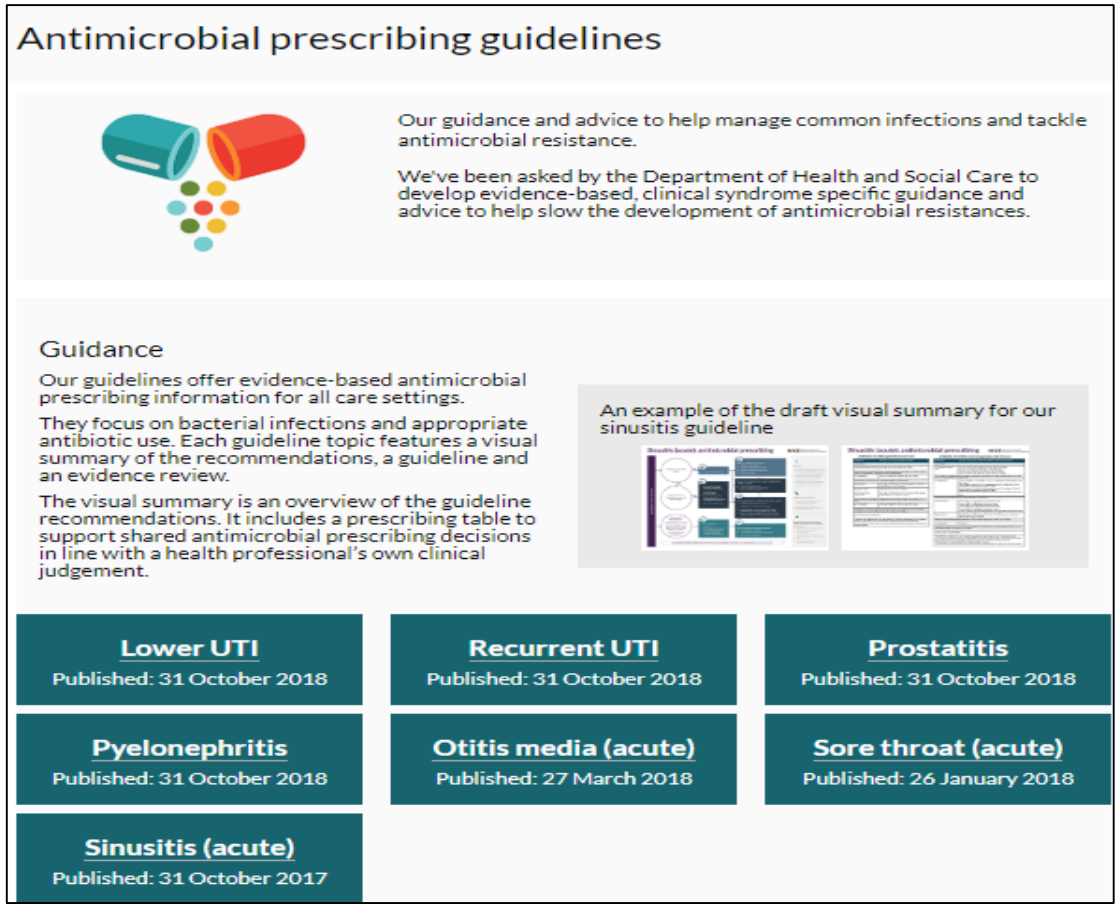
interpreted using oral Penicillin V breakpoints (≥2 µg/mL);

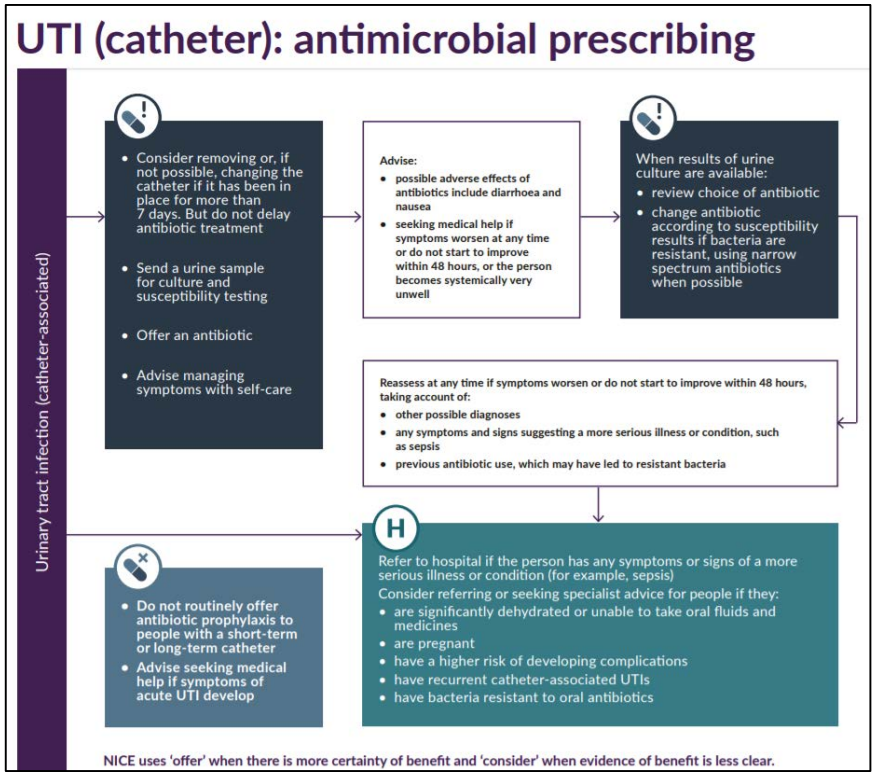
Including MIC≤0.06 mg/L (50.3%), MIC=0.12-1mg/L (28.6%), MIC=2mg/L (18.0) and 6 MIC=4 mg/L (3.1%).

+ Another 62% was ciprofloxacin-intermediate

MSSA, methicillin-sensitive *S. aureus*; MRSA, methicillin-resistant *S. aureus*; ESBL, extended-spectrum beta-lactamases

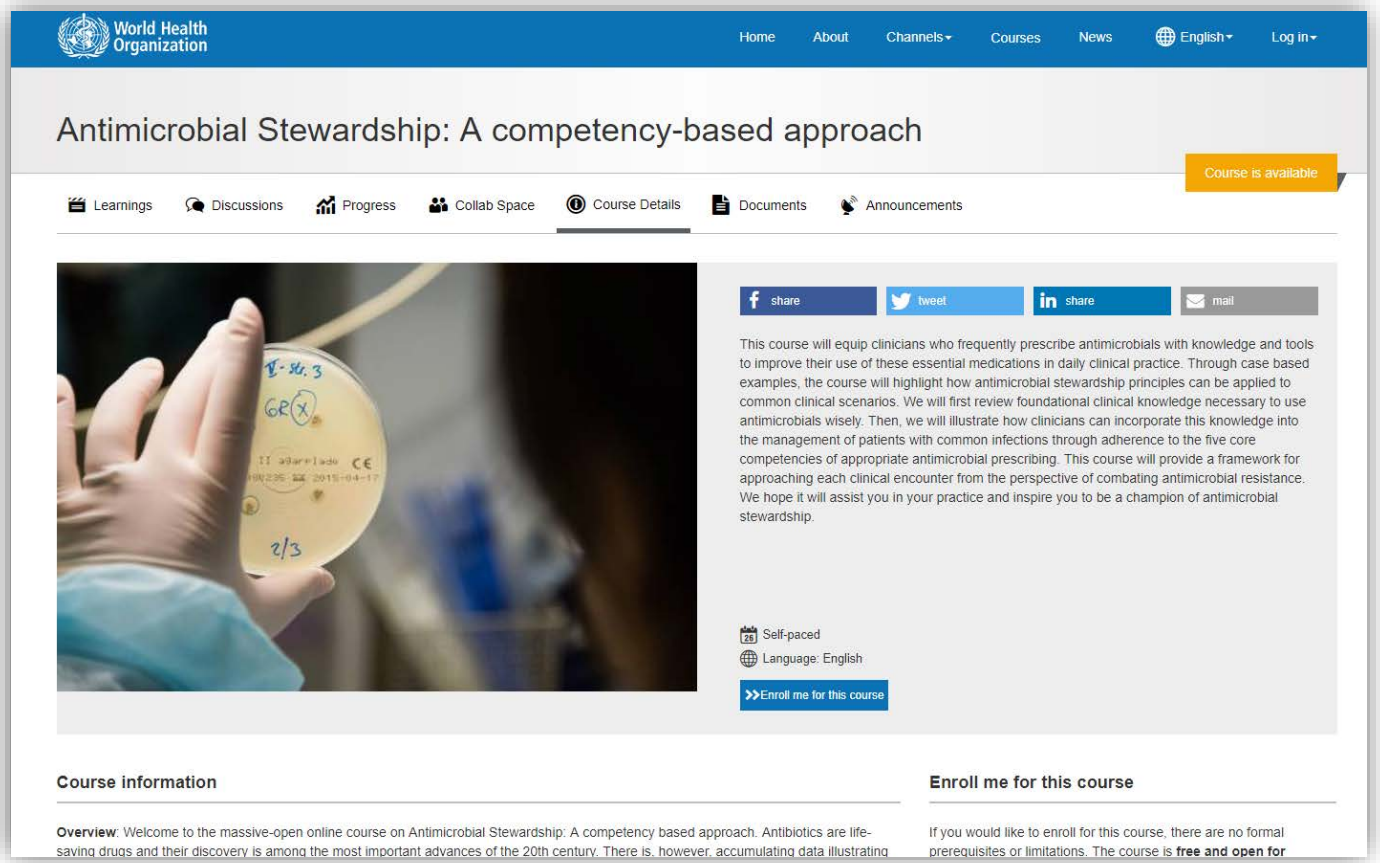
PRESCRIPTION GUIDELINES





https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines

LECTURES & TRAINING COURSES



ASP INTERVENTIONS EMPLOYED WORLDWIDE

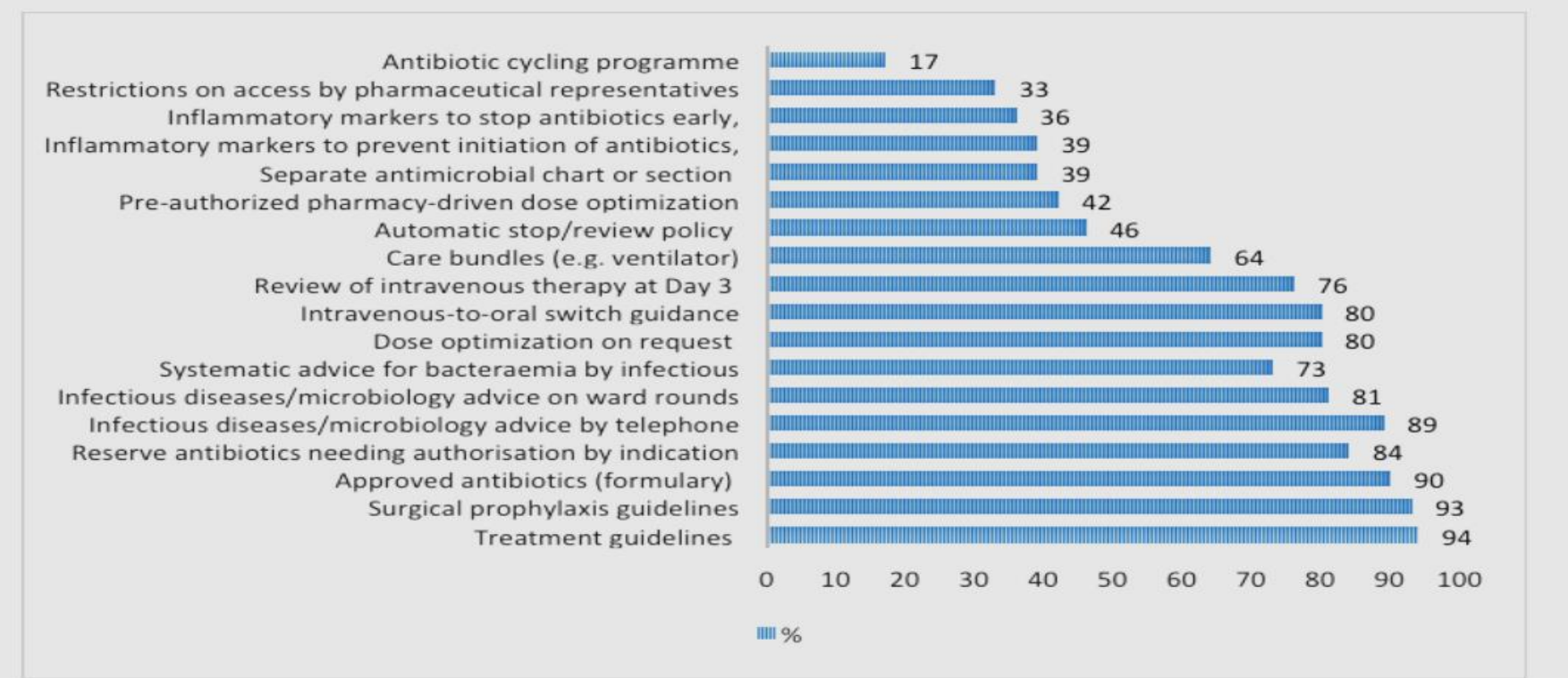


FIGURE 7
Results of a global survey on types of AMS interventions employed as part of an ASP

ANTIMICROBIAL STEWARDSHIP From Principles to Practice, BSAC

Core Elements of Outpatient Antibiotic Stewardship

The *Core Elements of Outpatient Antibiotic Stewardship* follow and are summarized in a clinician checklist (Figure 1) and a facility checklist (Figure 2):

Figure 1. Clinician Checklist for Core Elements of Outpatient Antibiotic Stewardship

CDC recommends that outpatient clinicians take steps to implement antibiotic stewardship activities. Use this checklist as a baseline assessment of policies and practices that are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually).

COMMITMENT

1. **Can you demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety related to antibiotics?** ❑ Yes ❑ No

   If yes, indicate which of the following are in place (select all that apply)
   - ❑ Write and display public commitments in support of antibiotic stewardship.

ACTION

2. **Have you implemented at least one practice to improve antibiotic prescribing?** ❑ Yes ❑ No

   If yes, indicate which practices which you use. (Select all that apply.)
   - ❑ Use evidence-based diagnostic criteria and treatment recommendations.
   - ❑ Use delayed prescribing practices or watchful waiting, when appropriate.

TRACKING AND REPORTING

3. **Do you monitor at least one aspect of antibiotic prescribing?** ❑ Yes ❑ No

   If yes, indicate which of the following are being tracked. (Select all that apply.)
   - ❑ Self-evaluate antibiotic prescribing practices.
   - ❑ Participate in continuing medical education and quality improvement activities to track and improve antibiotic prescribing.

EDUCATION AND EXPERTISE

4. **Do you provide education to patients and seek out continuing education on antibiotic prescribing?** ❑ Yes ❑ No

   If yes, indicate how you provide antibiotic stewardship education. (Select all that apply.)
   - ❑ Use eective communications strategies to educate patients about when antibiotics are and are not needed.
   - ❑ Educate about the potential harms of antibiotic treatment.
   - ❑ Provide patient education materials

Hong Kong Strategy and Action Plan on Antimicrobial Resistance 2017-2022

Objective 5 - Implement and enhance training in prescribing antimicrobials through ASP in human health sector

5.1	Ensure adequate resources for implementation and evaluation of ASP in healthcare settings	5.1.1	Assess resource implication for implementation of ASP	- DH - HA	On-going
5.2	Promote antibiotic prescription according to evidence-based guidelines for doctors and dentists	5.2.1	Continue to review and update the IMPACT guideline regularly for in-patient antibiotic stewardship and promulgate its use	- DH - HA	On-going
		5.2.2	Continue ASP in public hospitals	- DH - HA	On-going
		5.2.3	Advocate ASP in private hospitals	- DH - Private hospitals	On-going
		5.2.4	Formulate and promulgate evidence-based guidelines in primary care setting	- DH - HA - Professional bodies	Produce guideline by 2018

LAUNCHING OF ASP IN PRIMARY CARE IN HK

The Controller of the Centre for Health Protection of the Department of Health, Dr Wong Ka-hing, today (November 13) gives welcoming remarks at the Seminar on Antibiotic Stewardship Programme in Primary Care and Hospital Settings.

November 13, 2017

Membership of Advisory Group on Antibiotic Stewardship in Primary Care

Chairman

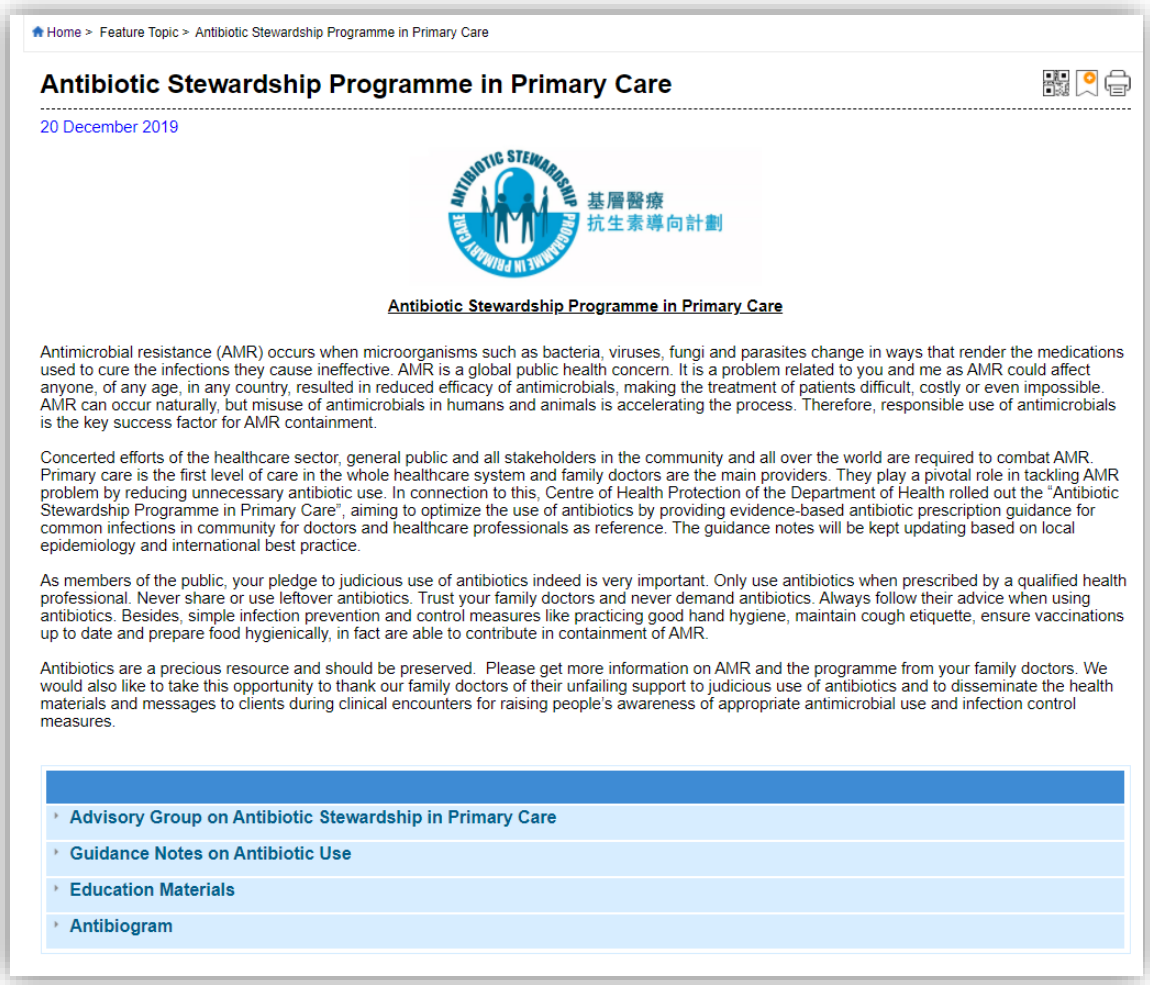
Dr Angus CHAN Ming-wai	(President, Hong Kong College of Family Physicians)

Members

Dr David CHAO Vai-kiong	(Chief of Service, Department of Family Medicine and Primary Health Care, United Christian Hospital)
Dr CHOI Kin	(President, Hong Kong Medical Association)
Dr CHOI Kin-wing	(Vice-president, Hong Kong Society for Infectious Diseases)
Dr CHOW Yat	(Executive Medical Director, Quality HealthCare Medical Services Limited)
Dr HO Pak-leung	(Chairman, IMPACT Editorial Board)
Dr Eric HUI Ming-tung	(Chief of Service (Family Medicine), New Territories East Cluster, Hospital Authority)
Dr KWONG Kin-hung	(Medical Director, Human Health Holdings Limited)
Mr Benjamin KWONG Yiu-sum	(Senior Pharmacist, Hospital Authority)
Professor LAM Tai-pong	(Professor, Department of Family Medicine and Primary Care, University of Hong Kong)
Professor Martin WONG Chi-sang	(Editor, Hong Kong Academy of Medicine)
Dr YEUNG Chiu-fat	(President, Hong Kong Doctors Union)
Professor Joyce YOU Hoi-sze	(Associate Professor, School of Pharmacy, Chinese University of Hong Kong)
Dr Raymond YUNG Wai-hung	(Specialist in Clinical Microbiology and Infection, Hong Kong Sanatorium & Hospital)

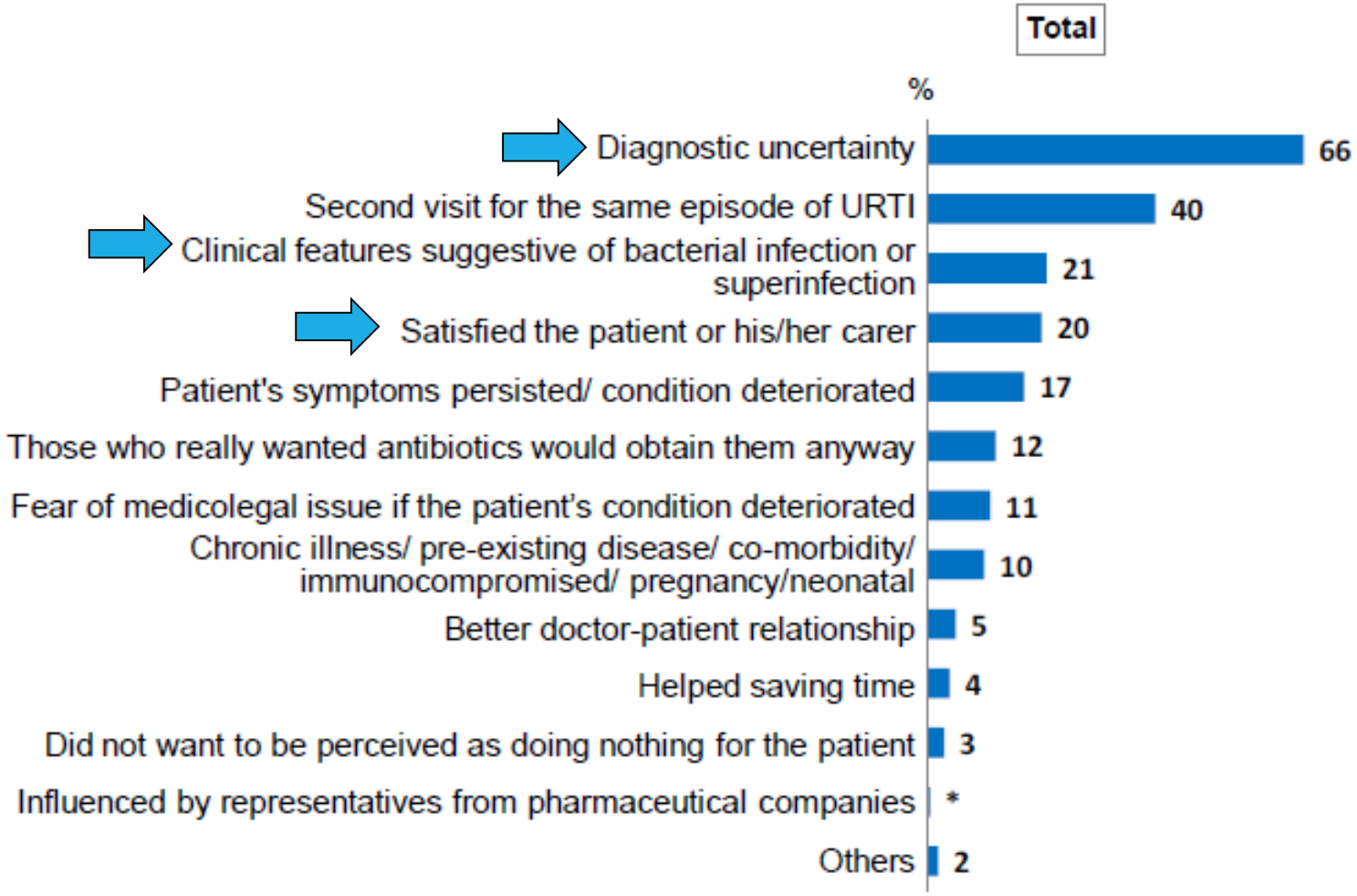
Ex-officio Members from Department of Health

Head, Infection Control Branch, Centre for Health Protection
Consultant (Antimicrobial Resistance), Centre for Health Protection
Head, Primary Care Office
Consultant (Family Medicine), Professional Development and Quality Assurance
Senior Medical and Health Officer (2), Infection Control Branch, Centre for Health Protection
Senior Medical and Health Officer (3), Infection Control Branch, Centre for Health Protection
Senior Pharmacist, Infection Control Branch, Centre for Health Protection



https://www.chp.gov.hk/en/features/49811.html

Reasons for prescribing antibiotics to patients with URTIs / cold / flu – I



Survey on Use of Antibiotics among Medical Doctors in Hong Kong. Dept of Health 2012.

GUIDANCE NOTES

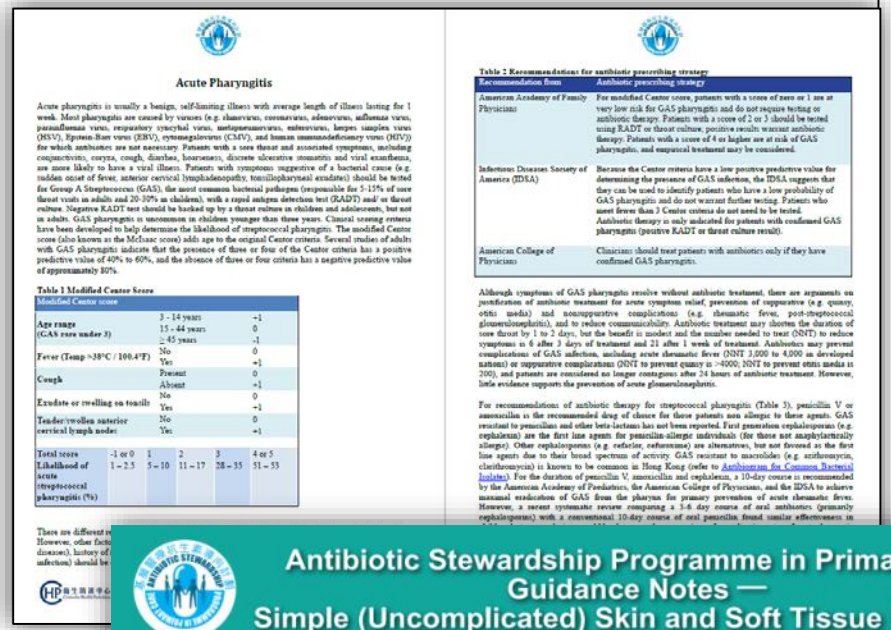
3 Guidance Notes published in 2017

- Acute Pharyngitis
- Uncomplicated Cystitis in Women
- Skin & Soft Tissue Infection

4 Guidance notes published in 2018

- Acute Otitis Media
- Acute Rhinosinusitis
- Community Acquired Pneumonia
- Acute Exacerbations in Chronic Obstructive Pulmonary Disease

FORMATS



Acute Pharyngitis

Acute pharyngitis is usually a benign, self-limiting illness with average length of illness lasting for 1 week. Most pharyngitis are caused by viruses (e.g. rhinovirus, coronavirus, adenovirus, influenza virus, parainfluenza virus, respiratory syncytial virus, metapneumovirus, enterovirus, herpes simplex virus (HSV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV)) for which antibiotics are not necessary. Patients with a sore throat and associated symptoms, including conjunctivitis, coryza, cough, diarrhea, hoarseness, discrete ulcerative stomatitis and viral exanthema, are more likely to have a viral illness. Patients with symptoms suggestive of a bacterial cause (e.g. sudden onset of fever, anterior cervical lymphadenopathy, tonsillopharyngeal exudates) should be tested for Group A Streptococcus (GAS), the most common bacterial pathogen (responsible for 5-15% of sore throat visits in adults and 20-30% in children), with a rapid antigen detection test (RADT) and/or throat culture. Negative RADT test should be backed up by a throat culture in children and adolescents, but not in adults. GAS pharyngitis is uncommon in children younger than three years. Clinical scoring criteria have been developed to help determine the likelihood of streptococcal pharyngitis. The modified Centor score (also known as the McIsaac score) adds age to the original Centor criteria. Several studies of adults with GAS pharyngitis indicate that the presence of three or four of the Centor criteria has a positive predictive value of 40% to 60%, and the absence of three or four criteria has a negative predictive value of approximately 80%.

Table 1 Modified Centor Score

Modified Centor score						
Age range (GAS rare under 3)		3 - 14 years				+1
		15 - 44 years				0
		≥ 45 years				-1
Fever (Temp >38°C / 100.4°F)		No				0
		Yes				+1
Cough		Present				0
		Absent				+1
Exudate or swelling on tonsils		No				0
		Yes				+1
Tender/swollen anterior cervical lymph nodes		No				0
		Yes				+1
Total score	-1 or 0	1	2	3	4 or 5	
Likelihood of acute streptococcal pharyngitis (%)	1 – 2.5	5 – 10	11 – 17	28 – 35	51 – 53	

There are different r... However, other facto... diseases), history of... infections) should be...

Table 2 Recommendations for antibiotic prescribing strategy

Recommendation from	Antibiotic prescribing strategy
American Academy of Family Physicians	For modified Centor score, patients with a score of zero or 1 are at very low risk for GAS pharyngitis and do not require testing or antibiotic therapy. Patients with a score of 2 or 3 should be tested using RADT or throat culture, positive results warrant antibiotic therapy. Patients with a score of 4 or higher are at risk of GAS pharyngitis, and empirical treatment may be considered.
Infectious Diseases Society of America (IDSA)	Because the Centor criteria have a low positive predictive value for determining the presence of GAS infection, the IDSA suggests that they can be used to identify patients who have a low probability of GAS pharyngitis and do not warrant further testing. Patients who meet fewer than 3 Centor criteria do not need to be tested. Antibiotic therapy is only indicated for patients with confirmed GAS pharyngitis (positive RADT or throat culture result).
American College of Physicians	Clinicians should treat patients with antibiotics only if they have confirmed GAS pharyngitis.

Although symptoms of GAS pharyngitis resolve without antibiotic treatment, there are arguments on justification of antibiotic treatment for acute symptom relief, prevention of suppurative (e.g. quinsy, otitis media) and nonsuppurative complications (e.g. rheumatic fever, post-streptococcal glomerulonephritis), and to reduce communicability. Antibiotic treatment may shorten the duration of sore throat by 1 to 2 days, but the benefit is modest and the number needed to treat (NNT) to reduce symptoms in 6 after 3 days of treatment and 21 after 1 week of treatment. Antibiotics may prevent complications of GAS infection, including acute rheumatic fever (NNT 3,000 to 4,000 in developed nations) or suppurative complications (NNT to prevent quinsy in >400; NNT to prevent otitis media is 200), and patients are considered no longer contagious after 24 hours of antibiotic treatment. However, little evidence supports the prevention of acute glomerulonephritis.

For recommendations of antibiotic therapy for streptococcal pharyngitis (Table 3), penicillin V or amoxicillin is the recommended drug of choice for those patients non allergic to these agents. GAS resistant to penicillins and other beta-lactams has not been reported. First generation cephalosporins (e.g. cephalexin) are the first line agents for penicillin-allergic individuals (for those not anaphylactic/atopic allergic). Other cephalosporins (e.g. cefaclor, cefuroxime) are alternatives, but not favored as the first line agents due to their broad spectrum of activity. GAS resistant to macrolides (e.g. azithromycin, clarithromycin) is known to be common in Hong Kong (refer to Antibiogram for Common Bacterial Isolates). For the duration of penicillin V, amoxicillin and cephalexin, a 10-day course is recommended by the American Academy of Paediatrics, the American College of Physicians, and the IDSA to achieve maximal eradication of GAS from the pharynx for primary prevention of acute rheumatic fever. However, a recent systematic review comparing a 5-6 day course of oral antibiotics (primarily cephalosporins) with a conventional 10-day course of oral penicillin found similar effectiveness in

Table 3 Recommended antibiotic treatment for acute streptococcal pharyngitis*

Drug (Route)	Dosage and Frequency, Adult (Usual)	Dosage and Frequency, Children (Usual)	Duration (Usual)	Remarks
First line				
Amoxicillin (oral)	1000 mg once daily or 500 mg two to three times daily	50 mg/kg (maximum = 1000 mg) once daily or 25 mg/kg (maximum = 500 mg) two to three times daily	5-7 days^	
Penicillin V (oral)	500 mg two to four times daily	If ≤27 kg: 250 mg two to three times daily If >27 kg: 500 mg two to four times daily	5-7 days^	
Cephalexin (oral)	500 mg two to four times daily	20 mg/kg (maximum = 500 mg) two to four times daily	5-7 days^	• Cephalosporins should be avoided in individuals with immediate (anaphylactic) type hypersensitivity to penicillin.
Second line				
Azithromycin (oral)	500 mg once daily	12 mg/kg (maximum = 500 mg) once daily	3 days^	• For individuals with penicillin allergy • Erythromycin resistant isolates are regarded as resistant to clarithromycin and azithromycin as well.
Clarithromycin (oral)	250 mg twice daily	7.5 mg/kg (maximum = 250 mg) twice daily	5 days^	• For individuals with penicillin allergy • Erythromycin resistant isolates are regarded as resistant to clarithromycin and azithromycin as well.

*Clinicians should tailor make drug treatment based on clinical judgement. Definitive t... based on microbiological and antibiotic sensitivity results if available.
^ For patients with positive laboratory results for GAS or certain special reasons (e.g... or known rheumatic heart disease), a l... mary prevention of acute rheumatic fever, ... V, cephalexin and clarithromycin, to a... as well.

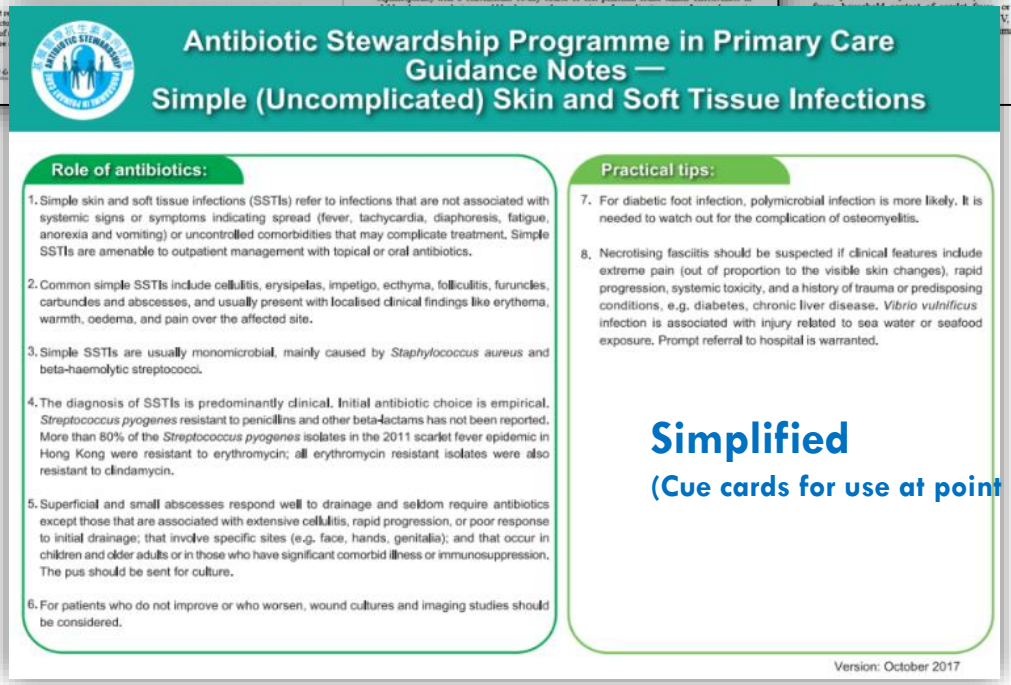
Page 3

Alternative diagnosis should be considered for patients who present with unusually severe signs and symptoms, such as difficulty swallowing, drooling, neck tenderness, or swelling. They should be evaluated for potential dangerous infections (such as peritonsillar abscess, retro/parapharyngeal abscess, and epiglottitis). Patients who do not improve within five to seven days or who have worsening symptoms, should be evaluated for a previously unsuspected diagnosis (e.g. infectious mononucleosis or primary HIV infection). Infectious mononucleosis is a clinical syndrome characterized by fever, severe pharyngitis (which lasts longer than pharyngitis due to GAS), cervical or diffuse lymphadenopathy, and prominent constitutional symptoms; patients who are treated with amoxicillin may develop a generalized, erythematous, maculopapular rash.

Management of patients with infections should be personalised. Doctors should check, document and get patients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.). They should be reminded to take antibiotics exactly as prescribed by their family doctors. If symptoms change, persist, or get worse, they should seek medical advice promptly.

References:

1. Shulman S, Bisno A, Clegg H, et al. Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2012;55(10):e86-e102.
2. Harris AM, Hicks LA, Qaseem A, High Value Care Task Force of the American College of Physicians and for the Centers for Disease Control and Prevention. Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. Ann Intern Med. 2016 Mar 15;164(6):425-34.
3. Cooper RJ, Hoffman JR, Bartlett JG, Besser RE, et al. Principles of Appropriate Antibiotic Use for Acute Pharyngitis in Adults: Background. Ann Intern Med. 2001;134:509-517.
4. Public Health England. Management and treatment of common infections. Antibiotic guidance for primary care: For consultation and local adaptation. 2017.
5. Choby BA. Diagnosis and Treatment of Streptococcal Pharyngitis. Am Fam Physician. 2009 Mar 1;79(5):383-90
6. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100. 2017.
7. Altamimi S, Khalaiwi KA, et al. Short-term late-generation antibiotics versus longer-term penicillin for acute streptococcal pharyngitis in children. Cochrane Database Syst Rev. 2012;8:CD004872.
8. C Chan, F Yau, F Cheng, et al. Practice Recommendation for the Management of Acute Pharyngitis. HK J Paediatr (New Series) 2015;20:156-162.
9. Centre for Health Protection, Department of Health. Statistics on laboratory surveillance: Bacterial ... 2014 – 2017.



Antibiotic Stewardship Programme in Primary Care
Guidance Notes —
Simple (Uncomplicated) Skin and Soft Tissue Infections

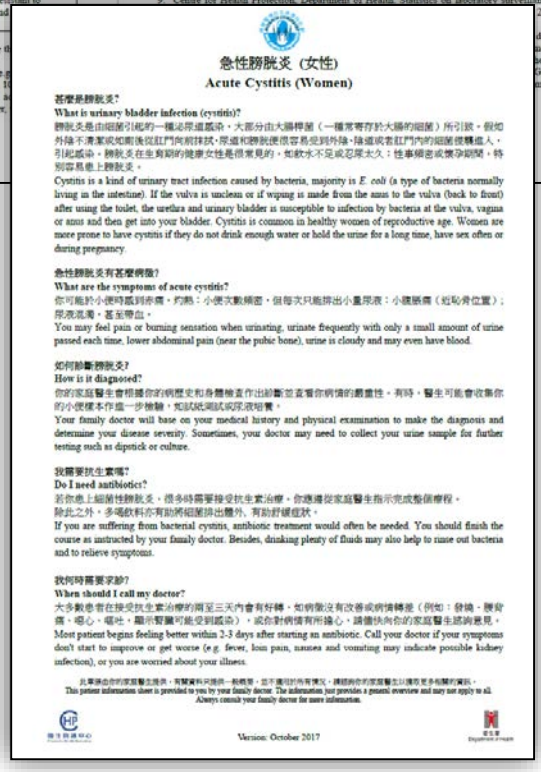
Role of antibiotics:

1. Simple skin and soft tissue infections (SSTIs) refer to infections that are not associated with systemic signs or symptoms indicating spread (fever, tachycardia, diaphoresis, fatigue, anorexia and vomiting) or uncontrolled comorbidities that may complicate treatment. Simple SSTIs are amenable to outpatient management with topical or oral antibiotics.
2. Common simple SSTIs include cellulitis, erysipelas, impetigo, ecthyma, folliculitis, furuncles, carbuncles and abscesses, and usually present with localised clinical findings like erythema, warmth, oedema, and pain over the affected site.
3. Simple SSTIs are usually monomicrobial, mainly caused by *Staphylococcus aureus* and beta-haemolytic streptococci.
4. The diagnosis of SSTIs is predominantly clinical. Initial antibiotic choice is empirical. *Streptococcus pyogenes* resistant to penicillins and other beta-lactams has not been reported. More than 80% of the *Streptococcus pyogenes* isolates in the 2011 scarlet fever epidemic in Hong Kong were resistant to erythromycin; all erythromycin resistant isolates were also resistant to clindamycin.
5. Superficial and small abscesses respond well to drainage and seldom require antibiotics except those that are associated with extensive cellulitis, rapid progression, or poor response to initial drainage; that involve specific sites (e.g. face, hands, genitalia); and that occur in children and older adults or in those who have significant comorbid illness or immunosuppression. The pus should be sent for culture.
6. For patients who do not improve or who worsen, wound cultures and imaging studies should be considered.

Practical tips:

7. For diabetic foot infection, polymicrobial infection is more likely. It is needed to watch out for the complication of osteomyelitis.
8. Necrotising fasciitis should be suspected if clinical features include extreme pain (out of proportion to the visible skin changes), rapid progression, systemic toxicity, and a history of trauma or predisposing conditions, e.g. diabetes, chronic liver disease. *Vibrio vulnificus* infection is associated with injury related to sea water or seafood exposure. Prompt referral to hospital is warranted.

Version: October 2017



急性膀胱炎（女性）
Acute Cystitis (Women)

甚麼是膀胱炎?
What is urinary bladder infection (cystitis)?

Cystitis is a kind of urinary tract infection caused by bacteria, majority is *E. coli* (a type of bacteria normally living in the intestine). If the vulva is unclean or if wiping is made from the anus to the vulva (back to front) after using the toilet, the urethra and urinary bladder is susceptible to infection by bacteria at the vulva, vagina or anus and then get into your bladder. Cystitis is common in healthy women of reproductive age. Women are more prone to have cystitis if they do not drink enough water or hold the urine for a long time, have sex often or during pregnancy.

急性膀胱炎有甚麼病徵?
What are the symptoms of acute cystitis?

You may feel pain or burning sensation when urinating, urinate frequently with only a small amount of urine passed each time, lower abdominal pain (near the pubic bone), urine is cloudy and may even have blood.

如何診斷膀胱炎?
How is it diagnosed?

Your family doctor will base on your medical history and physical examination to make the diagnosis and determine your disease severity. Sometimes, your doctor may need to collect your urine sample for further testing such as dipstick or culture.

我需要抗生素嗎?
Do I need antibiotics?

If you are suffering from bacterial cystitis, antibiotic treatment would often be needed. You should finish the course as instructed by your family doctor. Besides, drinking plenty of fluids may also help to rinse out bacteria and to relieve symptoms.

我何時需要求診?
When should I call my doctor?

Most patient begins feeling better within 2-3 days after starting an antibiotic. Call your doctor if your symptoms don't start to improve or get worse (e.g. fever, loin pain, nausea and vomiting may indicate possible kidney infection), or you are worried about your illness.

This patient information sheet is provided to you by your family doctor. The information just provides a general overview and may not apply to all. Always consult your family doctor for more information.

Version: October 2017

Full (Detailed explanations with references)

Simplified
(Cue cards for use at point of care)

Patient info sheet

Antibiotic Stewardship Programme in Primary Care

Guidance Notes — Acute Pharyngitis

Role of antibiotics:

1. Acute pharyngitis is usually a benign, self-limiting illness with average length of illness lasting for 1 week.
2. Viruses are the most common cause of acute pharyngitis. Presence of clinical features such as conjunctivitis, coryza, cough, diarrhoea, hoarseness, discrete ulcerative stomatitis and viral exanthema strongly suggest a viral etiology.
3. Group A Streptococcus (GAS) is the most common bacterial cause of acute pharyngitis, responsible for 5%-15% of sore throat visits in adults and 20%-30% in children from overseas. GAS pharyngitis is uncommon in children younger than three years.
4. Patients with symptoms suggesting a bacterial cause (e.g. sudden onset of fever, anterior cervical lymphadenopathy, tonsillopharyneal exudates) should be tested for GAS with a rapid antigen detection test (RADT) and/or throat culture. Negative RADT tests should be backed up by a throat culture in children and adolescents, but not in adults.
5. Alternatively, clinical scoring criteria (modified Centor score <Table 1>) have been developed to help determine the likelihood of streptococcal pharyngitis.
6. Empirical antibiotic treatment could be considered for highly suspected streptococcal cases (i.e. modified Centor score of 4 or 5). Antibiotic may shorten the duration of illness and prevent complications of GAS infection including acute rheumatic fever or suppurative complications (e.g. quinsy, otitis media).

Practical tips:

Table 1: Modified Centor score

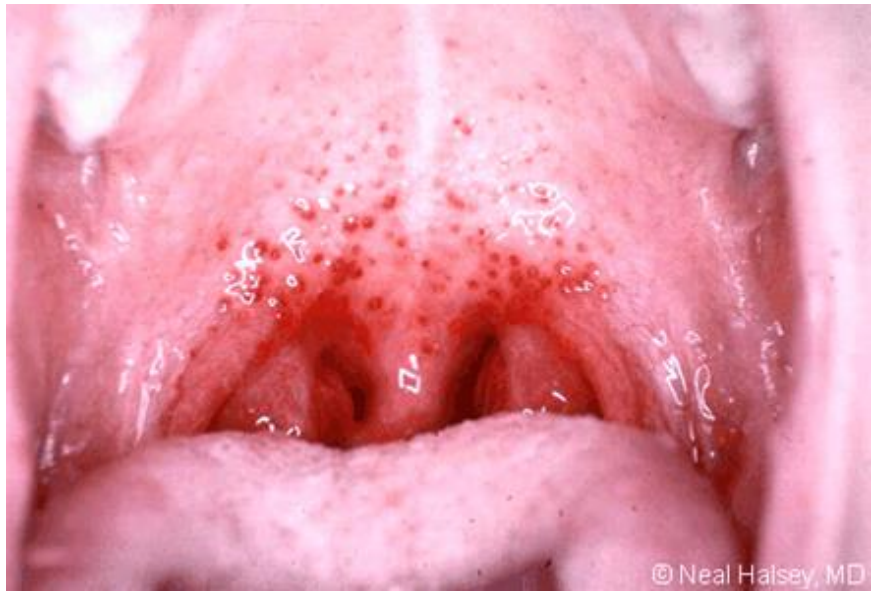
Age range (GAS rare under 3)	3 - 14 years 15 - 44 years ≥ 45 years	+1 0 -1
Fever (Temp >38˚C / 100.4˚F)	No Yes	0 +1
Cough	Present Absent	0 +1
Exudate or swelling on tonsils	No Yes	0 +1
Tender/swollen anterior cervical lymph nodes	No Yes	0 +1

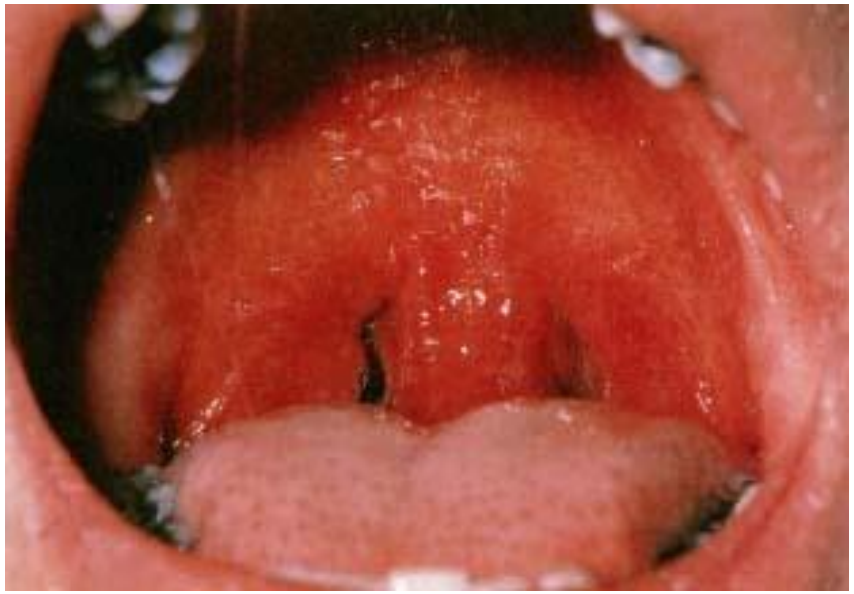
Total score	-1 or 0	1	2	3	4 or 5
Likelihood of acute streptococcal pharyngitis (%)	1 - 2.5	5 - 10	11 - 17	28 - 35	51 - 53

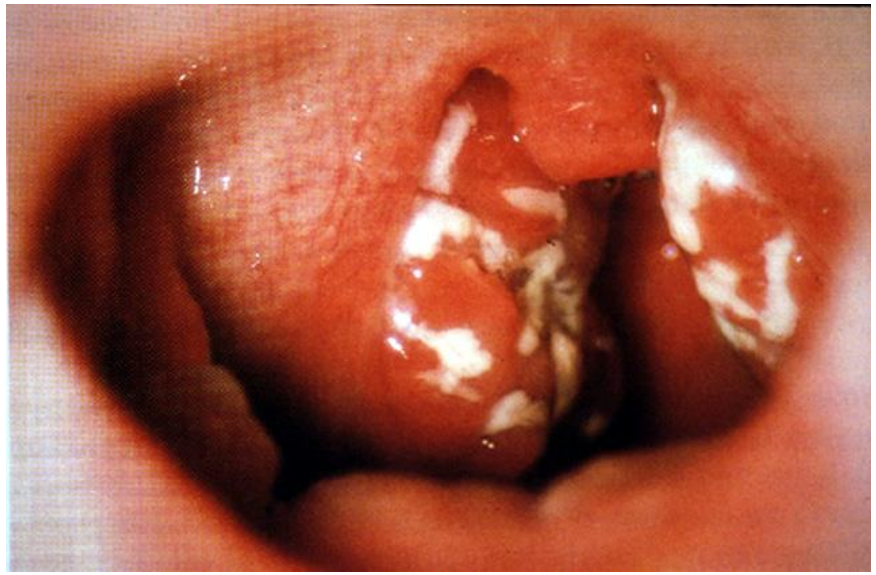
Version: October 2017

Causes of acute pharyngitis

	Estimated frequency, percent	Examples
Common bacterial pathogens	15	Group A streptococci
		Group C streptococci
		Group G streptococci
Less common bacterial pathogens	<5	*Chlamydophila pneumoniae* (TWAR)
		Mycoplasma pneumoniae
		Arcanobacterium haemolyticum
		Corynebactrium diphtheriae
		Fusobacterium necrophorum
		Neisseria gonorrheae
		Treponema pallidum
		Francisella tularensis
Viruses	50	Rhinovirus
		Adenovirus
		Influenza A and B
		Parainfluenza
		Coxsackievirus
		Coronavirus
		Echovirus
		Herpes simplex virus
		Epstein Barr virus
		Human immunodeficiency virus
		Cytomegalovirus
		Respiratory syncytial virus
		Metapneumovirus
No pathogen isolated	30	







RADT

Recommended antibiotic treatment for acute streptococcal pharyngitis*:

7. Penicillins and first generation cephalosporins are the first line agents in treating acute streptococcal pharyngitis. GAS resistant to penicillins and other beta-lactams has not been reported. GAS resistant to macrolides (e.g. azithromycin, clarithromycin) is known to be common in Hong Kong.

Drug (Route)	Dosage and Frequency, Adult (Usual)	Dosage and Frequency, Children (Usual)	Duration (Usual)	Remarks
First line				
Amoxicillin (oral)	1000 mg once daily or 500 mg two to three times daily	50 mg/kg (maximum = 1000 mg) once daily or 25 mg/kg (maximum = 500 mg) two to three times daily	5-7 days^	
Penicillin V (oral)	500 mg two to four times daily	If ⩽27 kg: 250 mg two to three times daily If >27 kg: 500 mg two to four times daily	5-7 days^	
Cephalexin (oral)	500 mg two to four times daily	20 mg/kg (maximum = 500 mg) two to four times daily	5-7 days^	• Cephalosporins should be avoided in individuals with immediate (anaphylactic) type hypersensitivity to penicillin.
Second line				
Azithromycin (oral)	500 mg once daily	12 mg/kg (maximum = 500 mg) once daily	3 days^	• For individuals with penicillin allergy. • Erythromycin resistant isolates are regarded as resistant to clarithromycin and azithromycin as well.
Clarithromycin (oral)	250 mg twice daily	7.5 mg/kg (maximum = 250 mg) twice daily	5 days^	• For individuals with penicillin allergy. • Erythromycin resistant isolates are regarded as resistant to clarithromycin and azithromycin as well.

* Clinicians should tailor-make drug treatment based on clinical judgement. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available.

^ For patients with positive laboratory results for GAS or certain special reasons (e.g. clinical scarlet fever, household contact of scarlet fever, or known rheumatic heart disease), a 10-day course is recommended for amoxicillin, penicillin V, cephalexin and clarithromycin, to achieve maximal eradication of GAS from the pharynx for primary prevention of acute rheumatic fever, whereas a 5-day course is recommended for azithromycin.

Antibiotic Stewardship Programme in Primary Care

Guidance Notes — Acute Uncomplicated Cystitis in Women

Role of antibiotics:

1. Acute uncomplicated cystitis in this Guidance Notes is defined as an uncomplicated lower urinary tract infection (UTI) in a pre-menopausal, non-pregnant woman with no known urological abnormalities or comorbidities.

2. In women who present with 1 or more symptoms of UTI, the probability of infection is approximately 50%. Specific combinations of symptoms (e.g. dysuria and frequency without vaginal discharge or irritation) raise the probability of UTI to more than 90%, effectively ruling in the diagnosis based on history alone.

3. Empirical antibiotic treatment is indicated based on clinical judgement. *Escherichia coli* is the predominant causative pathogen (80%).

4. Antibiotic treatment is not required for asymptomatic bacteriuria except in pregnancy or before urological procedures for which mucosal bleeding is anticipated.

Practical tips:

5. Family doctors should enquire about fever, flank pain, vaginal discharge, last menstrual period (LMP), and also patient's sexual history and past medical history (e.g. history of UTIs, diabetes mellitus, presence of indwelling urinary catheters, immunocompromised conditions, underlying urological abnormalities) which might be suggestive of a diagnosis other than simple bacterial cystitis (e.g. vaginitis, urethritis, structural urethral abnormalities, painful bladder syndrome (interstitial cystitis), pelvic inflammatory disease and nephrolithiasis).

6. Dipstick urinalysis can be useful to support the diagnosis if the clinical presentation is not typical. In women with uncomplicated UTI, the negative predictive value of urine dipstick testing when nitrite, leucocytes, and blood are all negative was 73%. The positive predictive value for having nitrite and either blood or leucocytes was 92%.

7. Urine cultures are recommended for women who present with atypical symptoms, or symptoms that do not resolve or that recur within two to four weeks after the completion of treatment, and for women with suspected acute pyelonephritis.

Version: October 2017

Bacterial pathogen isolation and percentage of antimicrobial resistance, out-patient setting, 2019

Urine specimens												
Organism	**Drugs / Resistance phenotype**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**
Escherichia coli	Ampicillin	69%	68%	67%	69%	68%	67%	69%	67%	67%	67%	68%
	Amoxicillin + clavulanic acid	6%	6%	5%	8%	6%	7%	7%	5%	5%	7%	6%
	Nalidixic acid	73%	70%	71%	73%	75%	71%	71%	76%	73%	71%	69%
	Nitrofurantoin	1%	1%	2%	2%	1%	2%	1%	1%	1%	1%	1%
	Co-trimoxazole	32%	35%	35%	36%	36%	30%	39%	34%	33%	34%	38%
	Levofloxacin[#]	33%	28%	32%	38%	37%	37%	34%	40%	34%	37%	35%
	ESBL+	18%	18%	18%	19%	18%	17%	18%	22%	17%	18%	21%
No. of isolates		488	464	548	469	538	527	613	615	593	596	494

Surveillance results from urinary specimens

Patient Demographic characteristics

- During the surveillance period, a total of 212 urine specimens were collected from patients with symptoms of urinary tract infection and fulfilling the selection criteria.
- Among all the patients, there were more female than male, of which 160 (75.5%) patients were female and 52 (24.5%) were male.
- Among the female patients being sampled, 31 (19.4%) belonged to the 55 - 64 age group, of which they contributed the largest proportion of sampled female patients. Similarly, a total of 8 (15.4%) male patients being sampled belonged to the 45 - 54 age group, of which they contributed the largest proportion of sampled male patients.

Culture results

- Among the 212 specimens, 87 (41.0%) of them were positive for bacterial culture.[2] A total of 90 bacterial isolates were obtained.[3]
- 57 (65.5%) isolates were identified as *Escherichia coli*, which was the commonest urinary pathogen detected among all positive specimens
- 7 (8.0%) isolates were identified as *Klebsiella pneumoniae*
- For other species, the three commonest isolates were *Proteus mirabilis* (6 isolates (6.9%)), *Citrobacter* species (5 isolates (5.7%)), and *Enterococcus* species (5 isolates (5.7%)).

Antimicrobial susceptibility test results

Resistance to the commonly used first-line oral antimicrobials

- None of the 57 *Escherichia coli* isolates was resistant to Nitrofurantoin. For *Klebsiella pneumoniae*, 1 (14.3%) out of 7 isolates was resistant to Nitrofurantoin.
- Regarding Amoxicillin/ Clavulanic acid, 3 (5.3%) of *Escherichia coli* and none of the *Klebsiella pneumoniae* isolates were resistant to this antimicrobial.

Resistance to second-line oral antimicrobials

- There were 23 (40.4%) *Escherichia coli* and 2 (28.6%) *Klebsiella pneumoniae* isolates tested resistant to Co-trimoxazole.
- There were 14 (24.6%) *Escherichia coli* and 1 (14.3%) *Klebsiella pneumoniae* isolates tested resistant to fluoroquinolones (Levofloxacin).

https://www.chp.gov.hk/en/static/103531.html

Recommended antibiotic treatment for acute uncomplicated cystitis in women*:

Drug (Route)	Dosage and Frequency (Usual)	Duration (Usual)	Remarks
First line			
Nitrofurantoin (oral)	50 mg four times daily	5-7 days	• Nitrofurantoin is an appropriate choice for therapy due to low local resistance rate and is less likely to select drug-resistant organisms. • It is contraindicated in patients with eGFR of less than 45 ml/minute.
Amoxicillin-clavulanate (oral)	250 mg/125 mg three times daily or 875 mg/125 mg twice daily	5-7 days	• Beta-lactam agents are appropriate choices for therapy even if there is intermediate susceptibility because they are physiologically concentrated in urine.
Second line			
Cefuroxime (oral)	500 mg twice daily	5-7 days	• Beta-lactam agents are appropriate choices for therapy even if there is intermediate susceptibility because they are physiologically concentrated in urine.
Levofloxacin (oral)	250 mg once daily	3 days	• Fluoroquinolones should be reserved for use in patients who have no other treatment options for acute uncomplicated cystitis because the risk of serious side effects (e.g. joint or tendon pain, muscle weakness, tingling or pricking sensation, numbness in the arms or legs, confusion, and hallucinations) generally outweighs the benefits.
Ciprofloxacin (oral)	250 mg twice daily	3 days	
Ofloxacin (oral)	200 mg twice daily	3 days	
Sulfamethoxazole-trimethoprim (oral)	960 mg twice daily	3 days	• Sulfamethoxazole-trimethoprim is not recommended as the first line agent given the high local resistance. • Beware of possible adverse reactions (e.g. skin rash).

* Clinicians should tailor-make drug treatment based on clinical judgement. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available.

The Department of Health gratefully acknowledges the invaluable support and contribution of the Advisory Group on Antibiotic Stewardship in Primary Care in the development of this guidance notes.

Antibiotic Stewardship Programme in Primary Care
Guidance Notes —
Simple (Uncomplicated) Skin and Soft Tissue Infections

Role of antibiotics:

1. Simple skin and soft tissue infections (SSTIs) refer to infections that are not associated with systemic signs or symptoms indicating spread (fever, tachycardia, diaphoresis, fatigue, anorexia and vomiting) or uncontrolled comorbidities that may complicate treatment. Simple SSTIs are amenable to outpatient management with topical or oral antibiotics.

2. Common simple SSTIs include cellulitis, erysipelas, impetigo, ecthyma, folliculitis, furuncles, carbuncles and abscesses, and usually present with localised clinical findings like erythema, warmth, oedema, and pain over the affected site.

3. Simple SSTIs are usually monomicrobial, mainly caused by *Staphylococcus aureus* and beta-haemolytic streptococci.

4. The diagnosis of SSTIs is predominantly clinical. Initial antibiotic choice is empirical. *Streptococcus pyogenes* resistant to penicillins and other beta-lactams has not been reported. More than 80% of the *Streptococcus pyogenes* isolates in the 2011 scarlet fever epidemic in Hong Kong were resistant to erythromycin; all erythromycin resistant isolates were also resistant to clindamycin.

5. Superficial and small abscesses respond well to drainage and seldom require antibiotics except those that are associated with extensive cellulitis, rapid progression, or poor response to initial drainage; that involve specific sites (e.g. face, hands, genitalia); and that occur in children and older adults or in those who have significant comorbid illness or immunosuppression. The pus should be sent for culture.

6. For patients who do not improve or who worsen, wound cultures and imaging studies should be considered.

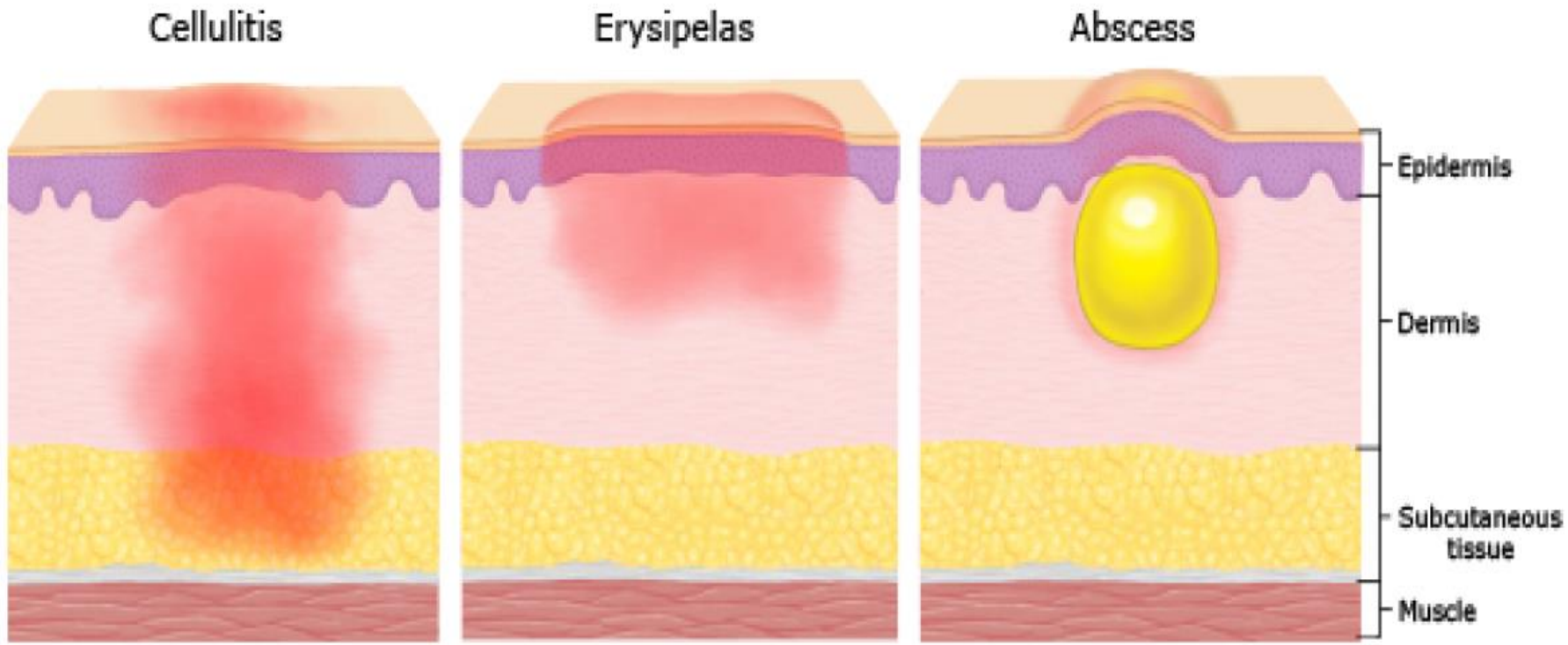
Practical tips:

7. For diabetic foot infection, polymicrobial infection is more likely. It is needed to watch out for the complication of osteomyelitis.

8. Necrotising fasciitis should be suspected if clinical features include extreme pain (out of proportion to the visible skin changes), rapid progression, systemic toxicity, and a history of trauma or predisposing conditions, e.g. diabetes, chronic liver disease. *Vibrio vulnificus* infection is associated with injury related to sea water or seafood exposure. Prompt referral to hospital is warranted.

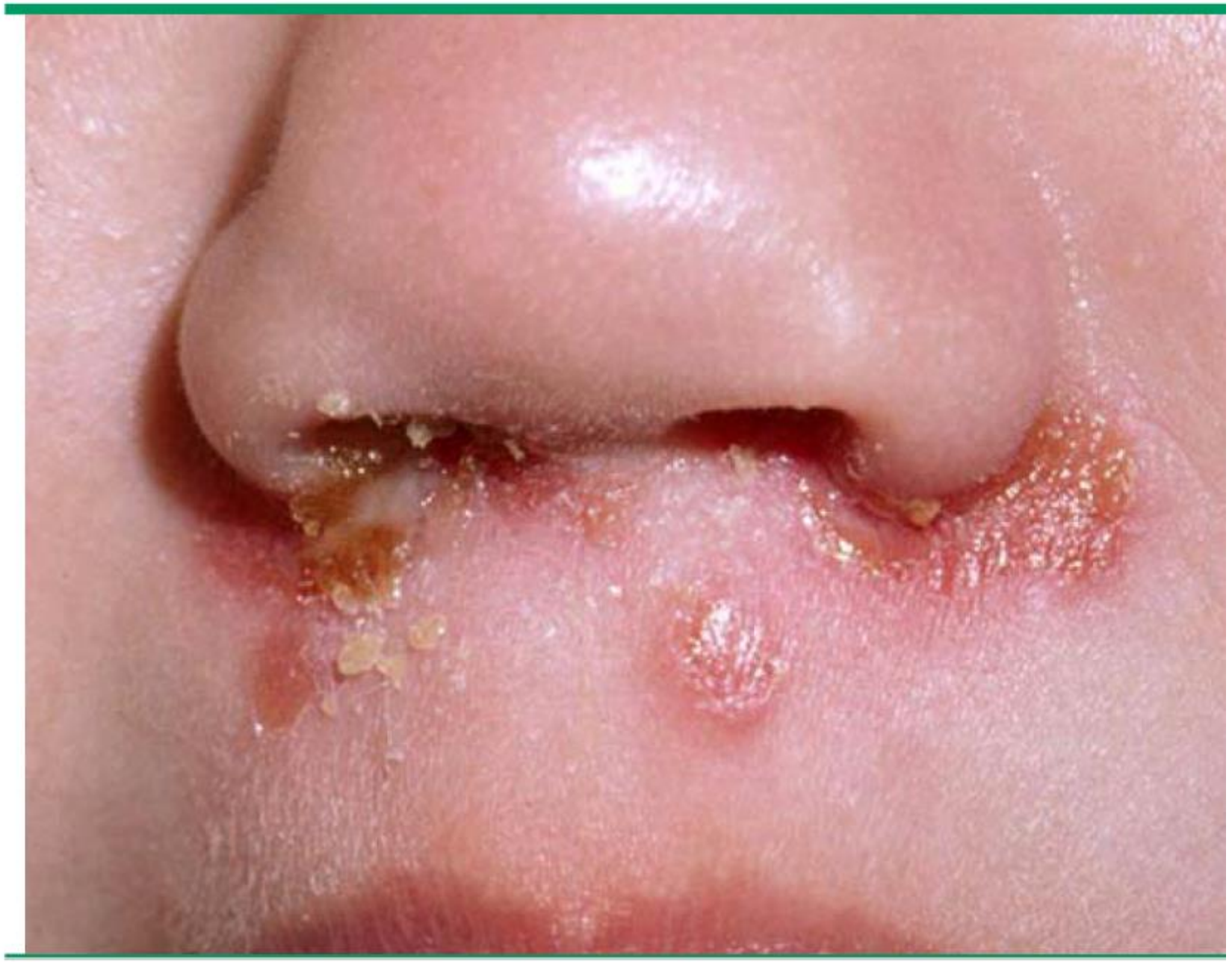
Version: October 2017

Skin anatomy: Cellulitis, erysipelas, and skin abscess



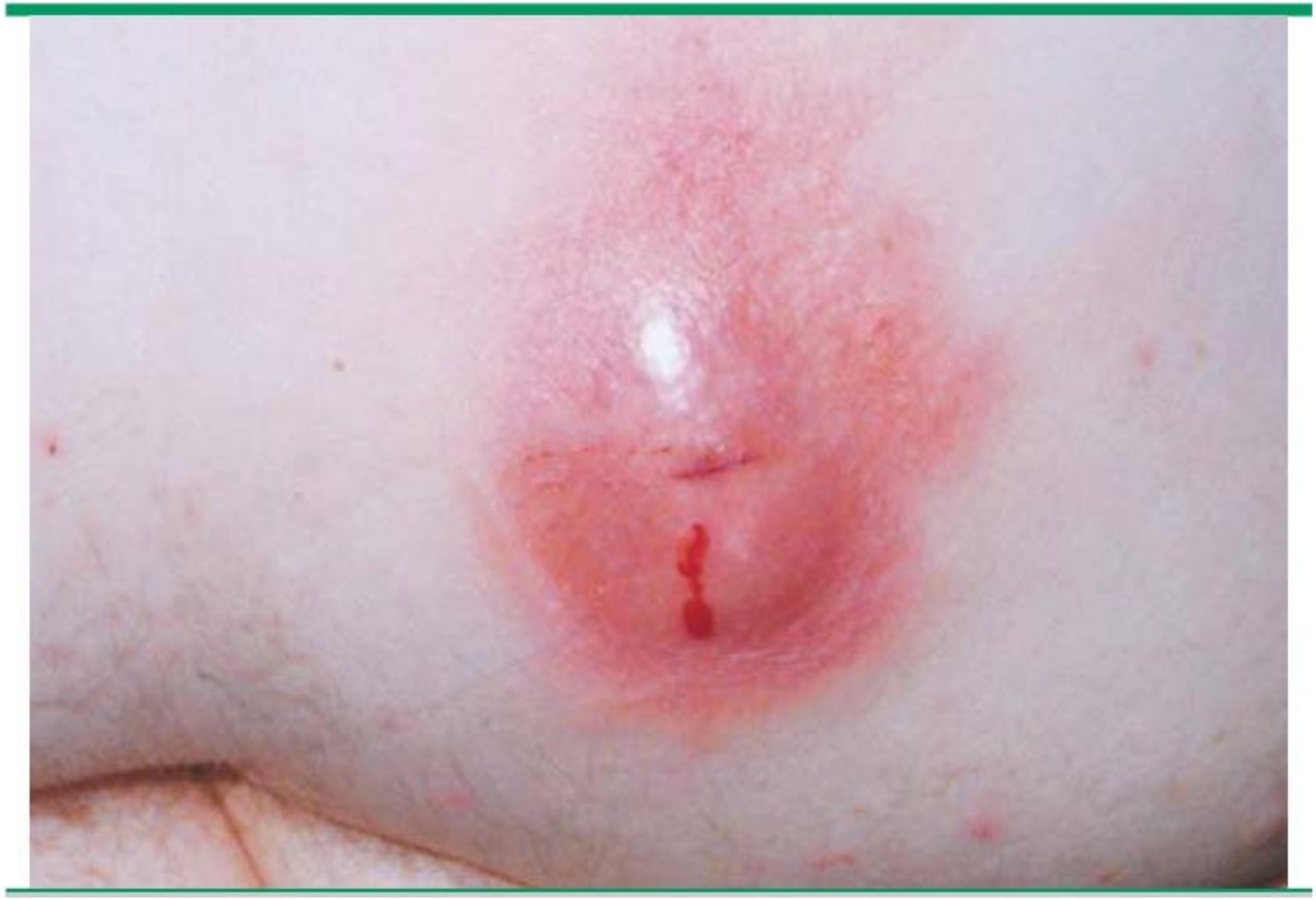
Cellulitis and erysipelas manifest as areas of skin erythema, edema, and warmth; they develop as a result of bacterial entry via breaches in the skin barrier. Cellulitis involves the deeper dermis and subcutaneous fat; in contrast, erysipelas involves the upper dermis, and there is clear demarcation between involved and uninvolved tissue. A skin abscess is a collection of pus within the dermis or subcutaneous space.

Nonbullous impetigo



Perinasal erythema, erosions, and crusts in a child with nonbullous impetigo.

Carbuncle



Carbuncle, which is a series of abscesses in the subcutaneous tissue that drain via hair follicles.

Recommended antibiotic treatment for simple skin and soft tissue infections*:

Drug (Route)	Dosage and Frequency, Adult (Usual)	Dosage and Frequency, Children^ (Usual)	Duration (Usual)	Remarks
Fusidic acid (topical)	Three times daily	Three times daily	5 days	• For mild and localised lesions of impetigo.
Cloxacillin (oral)	500 mg four times daily	Not available	5-10 days	• Good activity against methicillin sensitive *S. aureus* and some activity against beta-haemolytic streptococci.
Flucloxacillin (oral)	500 mg four times daily	1mth-2yr: 62.5-125 mg four times daily 2-10yr: 125-250 mg four times daily 10-18yr: 250-500 mg four times daily	5-10 days	• Good activity against methicillin sensitive *S. aureus* and some activity against beta-haemolytic streptococci.
Amoxicillin (oral)	500 mg three times daily	1mth-1yr: 62.5 mg three times daily 1-5yr: 125 mg three times daily 5-18yr: 250 mg three times daily	5-10 days	• Good activity against beta-haemolytic streptococci and no activity against *S. aureus*.
Amoxicillin-clavulanate (oral)	250 mg/125 mg three times daily or 875 mg/125 mg twice daily	25 mg/kg/day (maximum = 1750 mg/day) of the amoxicillin component in 2 divided doses	5-10 days	• Good activity against methicillin sensitive *S. aureus*, beta-haemolytic streptococci, some aerobic gram negative bacilli and some anaerobes.
Cephalexin (oral)	500 mg four times daily	25-50 mg/kg/day (maximum = 2000 mg/day) in 4 divided doses	5-10 days	• Good activity against methicillin sensitive *S. aureus* and beta-haemolytic streptococci. • For penicillin-allergic patients except those with immediate (anaphylactic) hypersensitivity reactions.
Levofloxacin† (oral)	500 mg once daily	Not recommended#	5-10 days	• Good activity against some aerobic gram negative bacilli, some activity against *S. aureus* and beta-haemolytic streptococci. • For penicillin-allergic patients.

* Clinicians should tailor-make drug treatment based on clinical judgement. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available.
^ Doses listed are not appropriate for neonates.
† Beware of possible serious side effects (e.g. joint or tendon pain, muscle weakness, tingling or pricking sensation, numbness in the arms or legs, confusion, and hallucinations).
# Fluoroquinolones are not recommended in children. However, after assessment of risks and benefits, levofloxacin can be considered a reasonable alternative for situations where no safe and effective substitute is available or in situations where the only alternative is parenteral therapy and levofloxacin offers an oral therapy option. Levofloxacin may be given orally at 8 mg/kg twice daily (maximum = 500 mg/day) for children aged ≥ 6 months and < 5 years, or at 8 mg/kg once daily (maximum = 500 mg/day) for children aged ≥ 5 years.

Antibiotic Stewardship Programme in Primary Care Guidance Notes
Acute Otitis Media

1. Acute otitis media (AOM) is a common paediatric condition caused by respiratory viruses and/or bacteria. The usual bacterial pathogens are *Streptococcus pneumoniae* (28%), *Haemophilus influenzae* (nontypeable) (23%) and *Moraxella catarrhalis* (7%).

2. Clinical features include ear pain, new-onset ear discharge, fever and irritability in infant. Otoscopy may show acute inflammation of the tympanic membrane with middle ear effusion. Bilateral ear infection is more likely bacterial in origin.

3. Diagnosis is established clinically. Serious complications e.g. meningitis and brain abscess are very rare in developed countries.

4. Antibiotics should be prescribed for children less than 6 months of age with suspected or confirmed AOM. For children older than 6 months, the decision to prescribe antibiotics would depend on clinical characteristics.

5. Analgesics e.g. paracetamol or ibuprofen should be given regardless of the decision for antibiotics.

6. If symptoms are persistent after 48 to 72 hours of observation, reassess for the presence of otitis media and consider initiation of antibiotics. For those not responding to initial antibiotics therapy, consider to change antibiotic or refer to specialists.

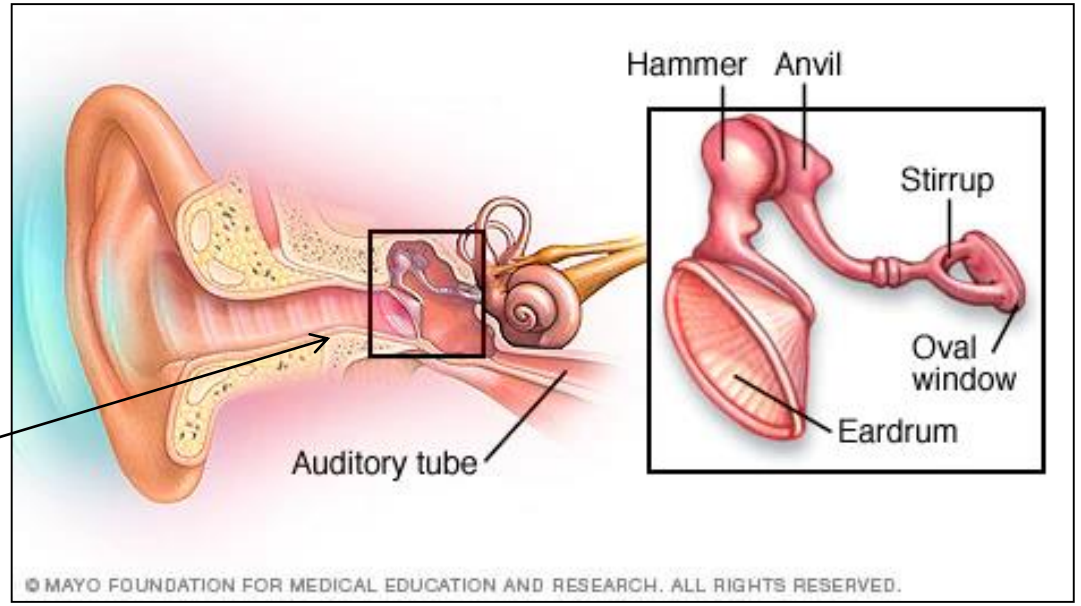
Table 1. Indications of antibiotic prescription and suggested duration of therapy for Acute Otitis Media in children -

Age and Clinical Characteristics	Recommended treatment approach
Children 6 months or older with otorrhoea or severe signs or symptoms (moderate or severe otalgia, otalgia for at least 48 hours, or temperature of 102.2˚F [39˚C] or higher)	Antibiotic therapy for 10 days
Children 6 to 23 months of age with bilateral acute otitis media without severe signs or symptoms	Antibiotic therapy for 10 days
Children 6 to 23 months of age with unilateral acute otitis media without severe signs or symptoms	Observation or antibiotic therapy for 10 days
Children 2 years or older without severe signs or symptoms	Observation or antibiotic therapy for 5-7 days

Version: November 2018 -

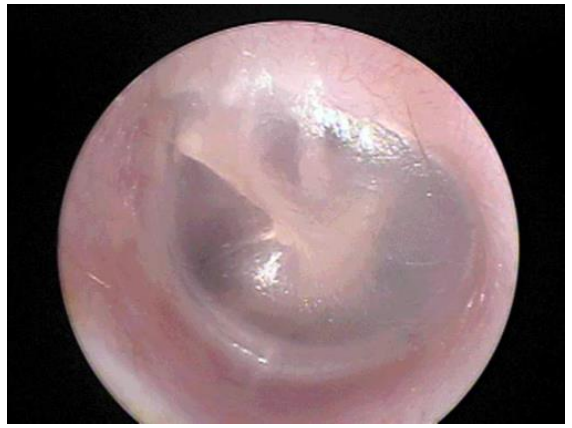
CLINICAL FEATURES

1. Otalgia interfering sleep and normal activities
2. Otorrhea (new-onset)
3. Fever
4. Irritability

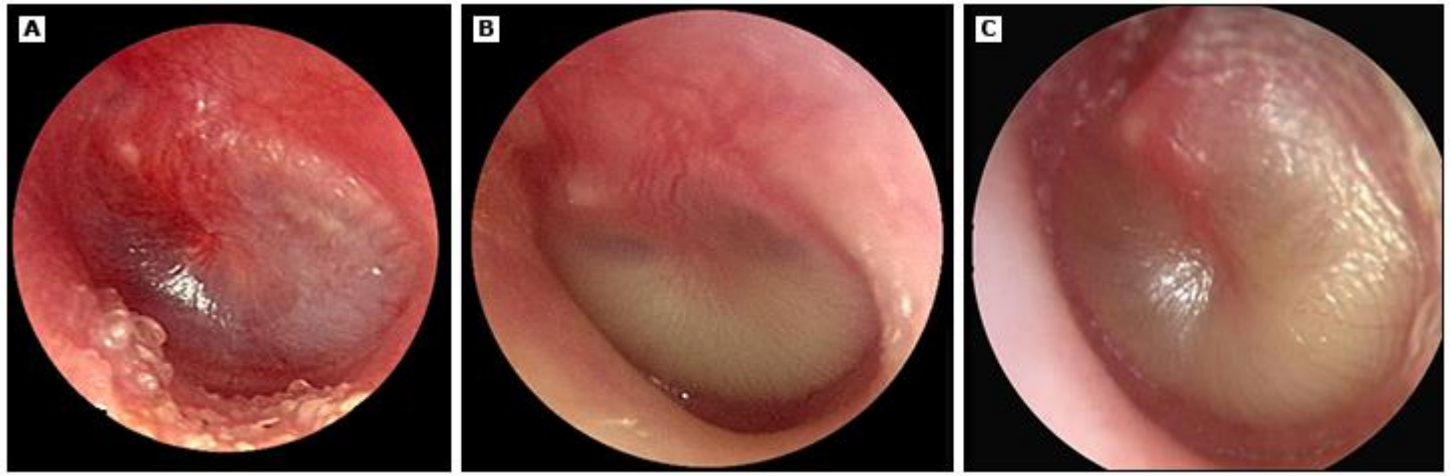


More suggestive of bacterial infection if:

- purulent otorrhoea
- Yellow & bulging tympanic membrane
- bilateral ear involvement
- High fever



Normal tympanic membrane



Uptodate

(A) Early acute otitis media with inflammation
(B) Purulent effusion with air-fluid level.
(C) Bulging purulent effusion filling the middle ear.

Discharge can be sent for culture & susceptibility testing

Most common bacterial pathogens:

- *Haemophilus influenzae*
- *Streptotoccus pneumoniae*
- *Moraxella catarrhalis*

Table 1. (*Continued*)

Countries/regions	OM	Age[a]	Size	Bacteria[b]			Ref.
				Hi	Spn	Mcat	
Thailand (2008–2009)	AOM	3m—5y	107	17.8%	24.3%	6.5%	[50]
Turkey (1998–2000)	AOM	6m—10y	78	14.1%	23.1%	5.1%	[51]
Turkey (2002–2004)	AOM	6m—12y	180	13.3%	25.6%	10.0%	[52]
Turkey (2003–2004)	AOM	6m—12y	120	13.3%	23.3%	8.3%	[53]
Average				**22.2%**	**26.4%**	**5.4%**	
Max				54.6%	49.9%	10.0%	
Min				5.0%	9.9%	1.2%	
Africa							
South Africa (1999)	AOM	2m—7y	173	5.2%	20.20%	1.20%	[54]
Average (all regions)				**23.1%**	**27.8%**	**7.0%**	
Max (all regions)				54.6%	49.9%	27.8%	
Min (all regions)				5.0%	9.9%	0.5%	

[a]: d = day; m = month; y = year;

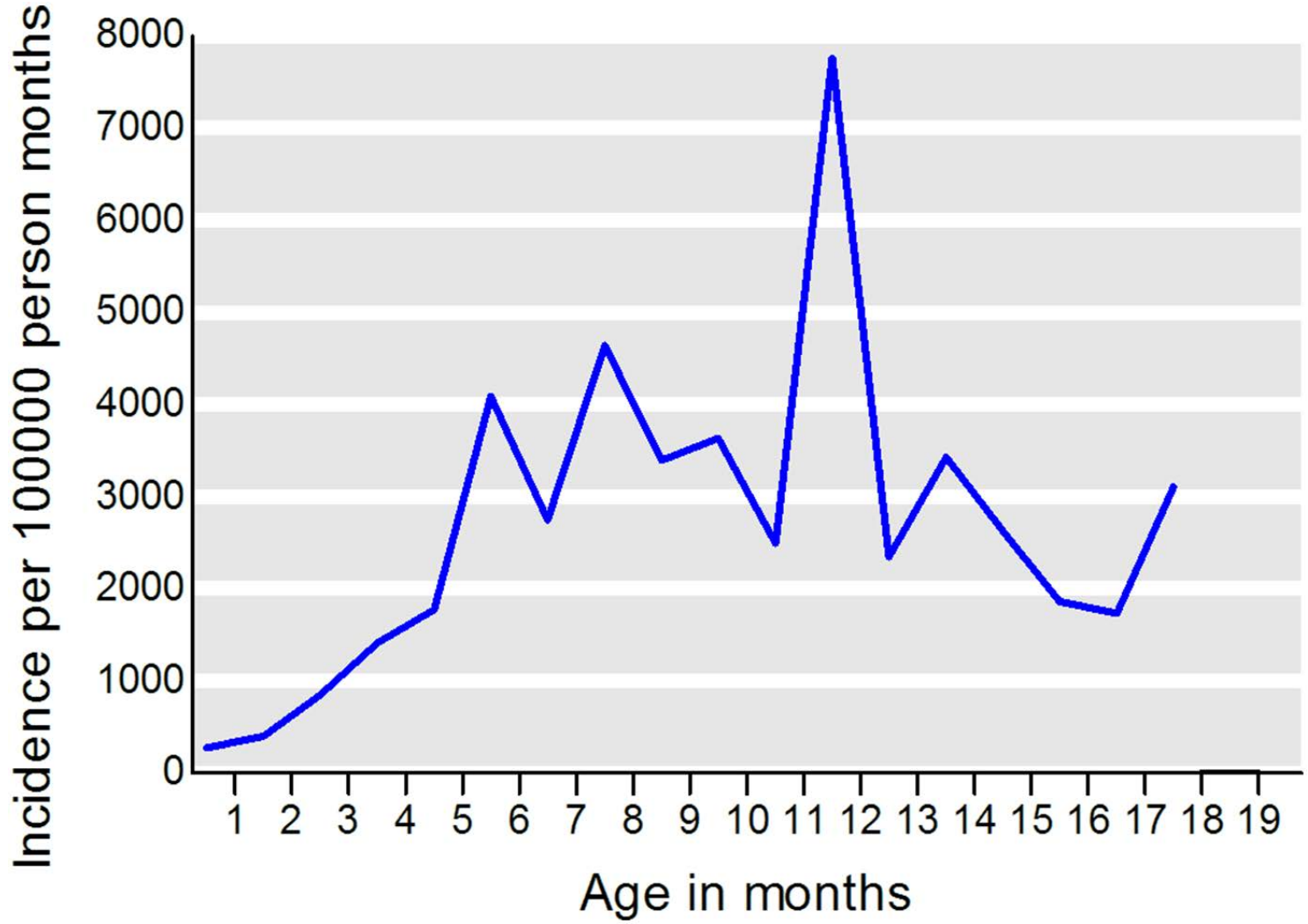
[b]: Hi: *H. influenzae*; Spn: *S. pneumoniae*; Mcat: *M. catarrhalis;*

[c] ND: Not detected

doi:10.1371/journal.pone.0150949.t001

Ngo CC, Massa HM, Thornton RB, Cripps AW (2016) Predominant Bacteria Detected from the Middle Ear Fluid of Children Experiencing Otitis Media: A Systematic Review. PLoS ONE 11(3)

AOM is most common at 6-18 months of age



Todberg T, Koch A, Andersson M, Olsen SF, Lous J, et al. (2014) Incidence of Otitis Media in a Contemporary Danish National Birth Cohort. PLOS ONE 9(12): e111732.

RECOMMENDED MANAGEMENT

Indications of antibiotic prescription and suggested duration of therapy for Acute Otitis Media in children

Age and Clinical Characteristics	Recommended treatment approach
Children 6 months or older with otorrhoea or severe signs or symptoms (moderate or severe otalgia, otalgia for at least 48 hours, or temperature of 102.2˚F [39˚C] or higher)	Antibiotic therapy for 10 days
Children 6 to 23 months of age with bilateral acute otitis media without severe signs or symptoms	Antibiotic therapy for 10 days
Children 6 to 23 months of age with unilateral acute otitis media without severe signs or symptoms	Observation or antibiotic therapy for 10 days
Children 2 years or older without severe signs or symptoms	Observation or antibiotic therapy for 5-7 days

Always prescribe antibiotics for infants < 6 months old

Table 2. Antibiotic recommendation for initial (first 48 to 72 hours) treatment of Acute Otitis Media in children# -

Severe illness e.g. fever >39°C, severe otalgia	Antibiotics recommended	Alternative antibiotics for penicillin allergy
No	**Amoxicillin** 80-90mg/kg per day in divided doses every 8 or 12 hours (maximum: 3000mg per day)	Non-type 1: **Cefuroxime**: 15 mg/kg/dose (maximum: 250 mg/dose) every 12 hours for infants > 3 months of age & Children <40kg; **Cefpodoxime**: 5 mg/kg/dose (maximum: 200 mg/dose) every 12 hours for Infants ≥ 2 months to Children <12 years of age Type 1 (rare): Macrolide e.g. **Azithromycin**, **Clarithromycin****
Yes	**Amoxicillin-clavulanate**^ (400mg/57mg per 5ml): 25 mg/3.6 mg/kg/day to 45 mg/6.4 mg/kg/day in divided doses every 12 hours; up to 70 mg/10 mg/kg/day in divided doses every 12 hours^^	Non-type 1: **Ceftriaxone**, 50 to 100 mg/kg/ day IV or IM in 1 to 2 divided doses every 12 or 24 hours (max 4000mg per day). Daily doses greater than 2g are divided into 2 doses.

Table 3. Antibiotic recommendation for failed initial treatment of Acute Otitis Media in children# -

Severe illness e.g. fever >39°C, severe otalgia	Antibiotics recommended	Alternative antibiotics for penicillin allergy
No	**Amoxicillin-clavulanate**^ (400mg/57mg per 5ml): 25 mg/3.6 mg/kg/day to 45 mg/6.4 mg/kg/day in divided doses every 12 hours; up to 70 mg/10 mg/kg/day in divided doses every 12 hours^^	Non-type 1: **Ceftriaxone**, 3 days; type 1 (rare): **Clindamycin**@
Yes	**Ceftriaxone**, 3 days	Referral to specialist

**Dosages of suggested macrolides are: Azithromycin: For children <15 kg (<3 years): 10 mg/kg once daily; For children ≥ 15 kg: 15-25 kg (3-7 years): 200 mg once daily; 26-35 kg (8-11 years): 300 mg once daily; 36-45 kg (12-14 years): 400 mg once daily; Over 45 kg: Dose as per adults
Clarithromycin: For children 6 months to 12 years of age: 7.5 mg/kg every 12 hours (maximum: 500 mg/dose).
^Amoxicillin-clavulanate is also indicated if 1) amoxicillin has been used in recent 30 days 2) purulent conjunctivitis is present as *H. influenzae* and *M. catarrhalis* are expected (cefuroxime is an alternative).
^^No clinical data are available for doses higher than 45 mg/6.4 mg per kg per day in children under 2 years and for all doses in infants under 2 months of age. Dosing recommendations cannot be made in these situations.
@Dosage of clindamycin in children is: 30 to 40 mg/kg/day in divided doses every 6 to 8 hours. Only capsule (not syrup) preparation is available locally. The capsule is dosed as 150mg each.
#The route of administration for all antibiotics recommended is oral except for ceftriaxone which is administered parenterally
Clinicians should tailor-make drug treatment based on clinical judgment. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available. -
Management of outpatients with infections should be individualised. Doctors should check, document and get outpatients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.). Outpatients should be reminded to take antibiotics exactly as prescribed by their family doctors.

Antibiotic Stewardship Programme in Primary Care Guidance Notes
Acute Rhinosinusitis

1. Acute rhinosinusitis (ARS) is usually caused by viruses associated with common colds. Less than 10% of them develops secondary bacterial infections.

2. The top three bacterial pathogens for acute bacterial rhinosinusitis (ABRS) are *Streptococcus pneumoniae*, *Haemophilus influenzae* (nontypeable) and *Moraxella catarrhalis*. Less commonly encountered bacteria include *Staphylococcus aureus*, non-pneumococcal streptococci and anaerobes.

3. ABRS is diagnosed clinically on the basis of persistent symptoms or signs > 10 days **plus** at least three of the following features: (1) discoloured nasal discharge (2) severe local pain (3) Fever (> 38ºC) or (4) a "double-sickening" clinical course

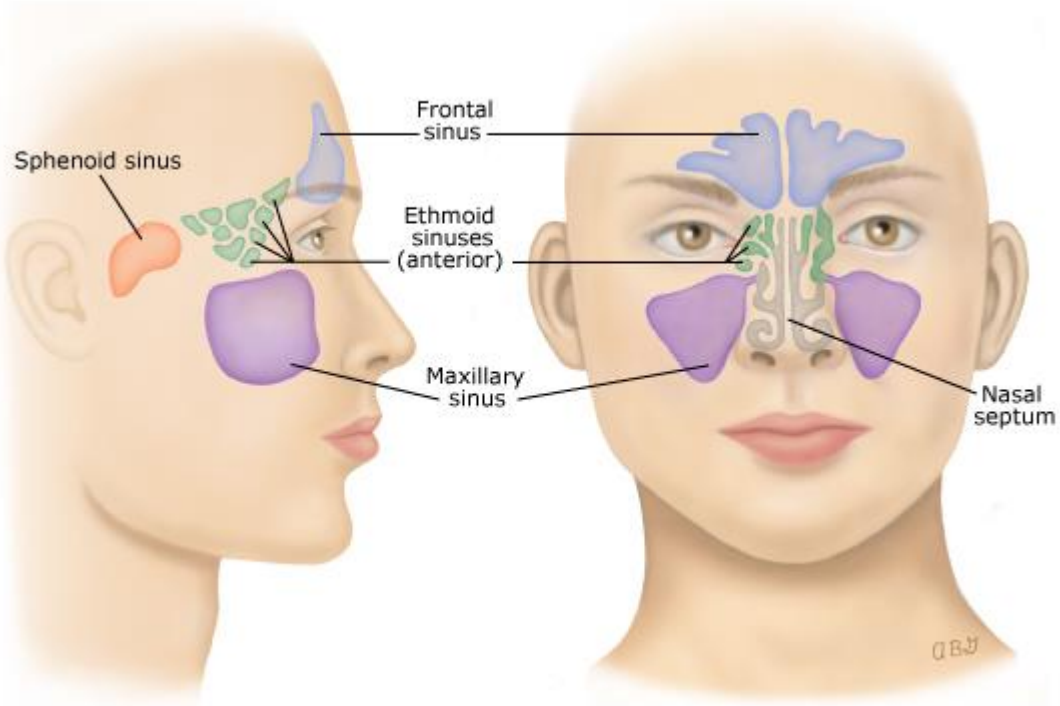
4. Routine treatment of mild and uncomplicated ARS cases with antibiotics is unwarranted. Antibiotics should be reserved for cases diagnosed as ABRS.

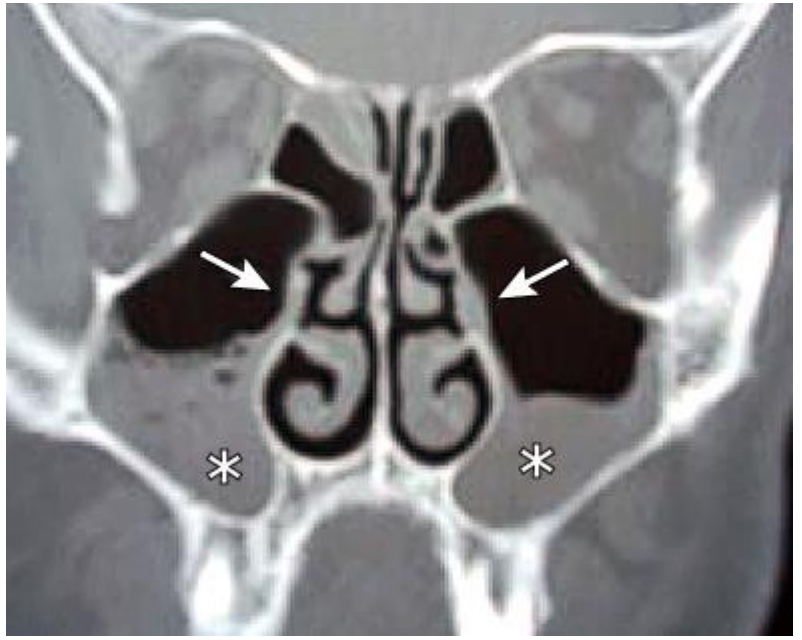
5. Useful adjunctive treatments for symptomatic relief include normal saline irrigation of the nasal cavity, paracetamol and NSAIDs.

Table 1. Antibiotic recommendation for treatment of Acute Bacterial Rhinosinusitis in adults

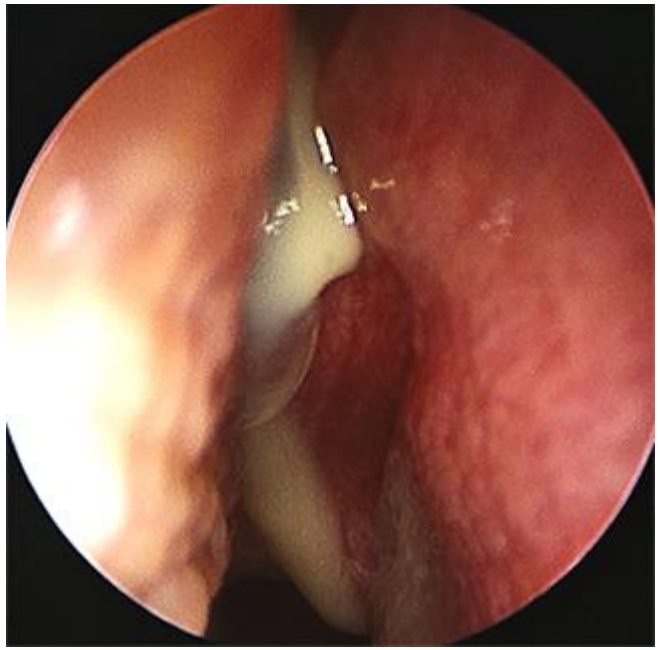
Drug (Route)	Dosage and Frequency, Adults (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin (oral)	500 or 1000 mg three times daily	5-10 days	High dose to cover *S. pneumoniae* with reduced penicillin susceptibility.*
Amoxicillin-clavulanate or other BLBLIs# (oral)	375mg (250mg/125mg) three times daily or 1g (875mg/125mg) twice daily	5-10 days	
Second line			
Levofloxacin† (oral)	500mg once daily	5-10 days	For severe (type 1) penicillin allergy (rare). **Contraindicated in paediatric population.**
Doxycycline (oral)	100mg twice daily or 200mg once daily	5-10 days	For severe (type 1) penicillin allergy (rare). **Contraindicated in children < 8 years old.**
Azithromycin (oral)	500mg once daily for 3 days or 500mg once daily for 1 day, then 250mg once daily for 4 days	3-5 days	For severe (type 1) penicillin allergy (rare). High rate of resistance in Hong Kong, follow up after initial course of antibiotic recommended.
Metronidazole (oral)	400mg three times daily	5-10 days -	As combination therapy with other antibiotics (except BLBLIs#) if anaerobes are suspected (e.g. in odontogenic infections).

Version: November 2018 -





Acute bacterial rhinosinusitis. Coronal image from a CT of the paranasal sinuses showing mucosal edema (arrows) and thick secretions (asterisks).



Endoscopic image of purulent drainage from the middle meatus in a patient with acute bacterial rhinosinusitis

Uptodate

Symptoms of acute rhinosinusitis

Purulent anterior nasal discharge
Purulent or discolored posterior nasal discharge
Nasal congestion or obstruction
Facial congestion or fullness
Hyposmia or anosmia
Fever
Headache
Ear pain, pressure, or fullness
Halitosis
Dental pain
Fatigue

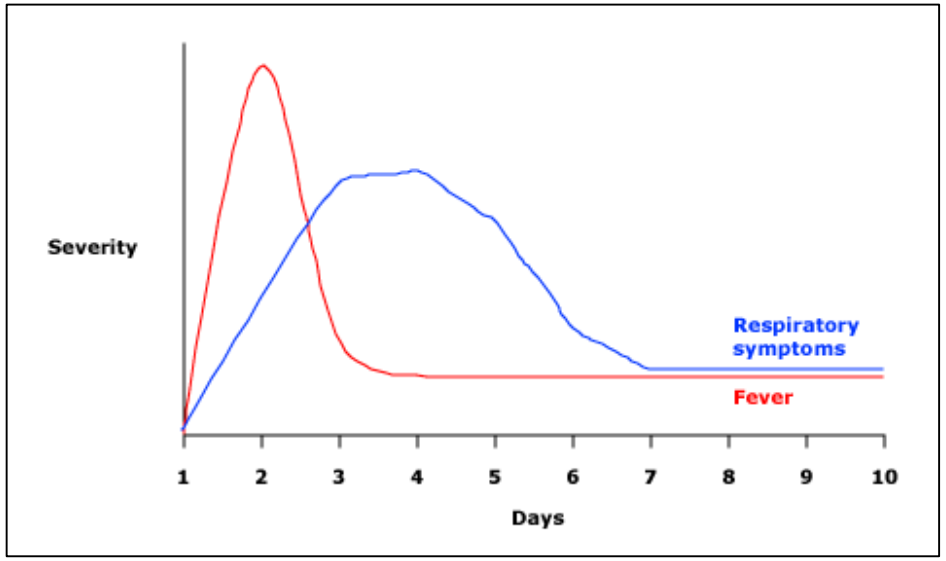
Reference:

1. *Chow AW, Benninger MS, Brook I, et al. IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults. Clin Infect Dis 2012; 54:e72.*

Acute rhinosinusitis are very commonly associated with URTIs

Features suggestive of secondary bacterial infection:

- Duration > 10 days
- Biphasic course ('double-sickening')
- Severe symptoms (fever, purulence of discharge, pain)



The course of uncomplicated viral URTI is 5-10 days

TABLE 58-3 Bacterial Etiology of Acute Sinusitis

	Adults ($N = 339$)		Children ($N = 30$)	
Organism	*Number of Isolates*	*% of Isolates*	*Number of Isolates*	*% of Isolates*
Streptococcus pneumoniae	92	41	17	41
Haemophilus influenzae	79	35	11	27
Anaerobes	16	7		
Streptococcal species	16	7	3	7
Moraxella catarrhalis	8	4	9	22
Staphylococcus aureus	7	3		
Other	8	4	1	2

Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th Edition

Nasal and throat swabs do not correlate well with underlying pathogens.
Treatment is mostly empirical

Table 2. Antibiotic recommendation for treatment of Acute Bacterial Rhinosinusitis in children -

Drug (Route)	Dosage and Frequency, Children (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin (oral)	45 mg/kg/day or 90 mg/kg/day (maximum: 3000 mg/day) in divided doses every 8 or 12 hours	10-14 days	High dose to cover *S. pneumoniae* with reduced penicillin susceptibility.^
Amoxicillin-clavulanate or other BLBLIs# (oral)	Children < 40 kg: 20mg (amoxicillin)/ 5mg (clavulanate)/kg/day to 60mg (amoxicillin) / 15mg (clavulanate)/kg/day in divided doses every 8 hours ##	10-14 days	
Second line			
Cefpodoxime (oral)	Infants ≥2 months to Children <12 years of age: Oral: 5 mg/kg/dose (maximum: 200 mg/dose) every 12 hours Children ≥12 years of age and Adolescents: refer to adult dosing	10-14 days	For non-type 1 penicillin allergy. Certain *S. pneumoniae* isolates may not be reliably covered by oral cephalosporins in the local setting.
Cefuroxime (oral)	Infants >3 months of age and Children: 15 mg/kg/dose (maximum : 250 mg/dose) every 12 hours	10-14 days	
Clarithromycin (oral)	Children 6 months to 12 years of age: 7.5 mg/kg every 12 hours (maximum: 500 mg/dose)	10-14 days	For severe (type 1) penicillin allergy (rare). High rate of resistance in Hong Kong, follow up after initial course of antibiotic recommended.
Azithromycin (oral)	For children <15 kg (<3 years): 10 mg/kg once daily For children ≥ 15 kg: 15-25 kg (3-7 years): 200 mg once daily; 26-35 kg (8-11 years): 300 mg once daily; 36-45 kg (12-14 years): 400 mg once daily; Over 45 kg: Dose as per adults	3-5 days	
Metronidazole (oral)	30 mg/kg/day in divided doses every 8 hours (maximum: 2000mg per day)	10-14 days	As combination therapy with other antibiotics (except BLBLIs#) if anaerobes are suspected (e.g. in odontogenic infections).

* Risk factors for drug-resistant *S. pneumoniae* (DRSP) in adults are age >65 years, beta-lactam therapy within past 3 months, alcoholism, multiple medical comorbidities, exposure to a child in a daycare centre.
^ Risk factors for drug-resistant *S. pneumoniae* (DRSP) in children are: Age < 2 years, beta-lactam therapy within past 3 months, daycare attendance and unimmunized with pneumococcal conjugate vaccine.
† Due to risk of serious side effects involving tendons, muscles, joints, nerves and the central nervous system, fluoroquinolones should be reserved for use in patients who have no alternative treatment options.
# Beta-lactam-beta-lactamase inhibitor combinations e.g. ampicillin-sulbactam.
No clinical data are available on doses higher than 40 mg/10 mg/kg per day in children under 2 years.
Clinicians should tailor-make drug treatment based on clinical judgment. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available.
Management of outpatients with infections should be individualised. Doctors should check, document and get outpatients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.). Outpatients should be reminded to take antibiotics exactly as prescribed by their family doctors.

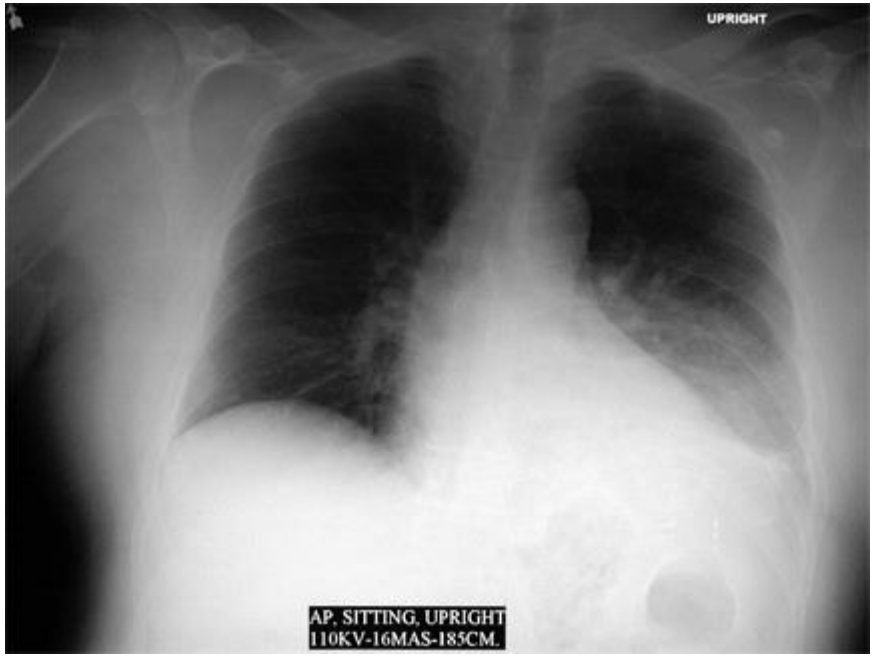
Antibiotic Stewardship Programme in Primary Care Guidance Notes
Community-Acquired Pneumonia

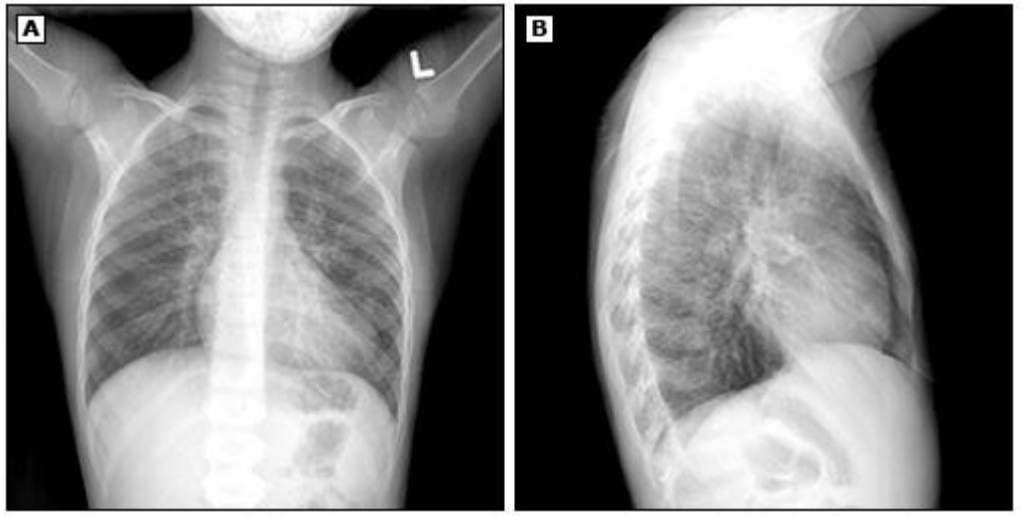
1. In the outpatient setting, the most frequently detected pathogens are *Streptococcus pneumoniae*, *Mycoplasma pneumoniae* and respiratory viruses (e.g. influenza, parainfluenza, respiratory syncytial virus). Less frequent causes include *Haemophilus influenzae* and *Moraxella catarrhalis*. Group A *Streptococcus* and *Staphylococcus aureus* may cause secondary bacterial pneumonia following influenza.
2. Antibiotic therapy should be started as soon as possible once the diagnosis of CAP is suspected or established.

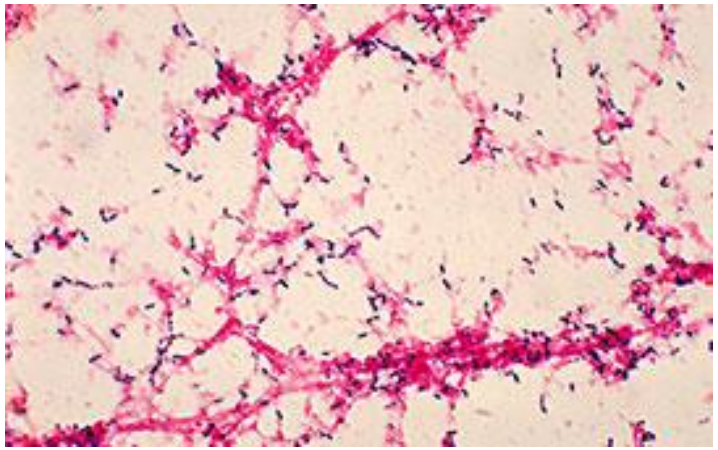
Table 1. Antibiotic recommendation for treatment of Community-Acquired Pneumonia in adults

Drug (Route)	Dosage and Frequency, Adults (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin (oral)	500 or 1000 mg three times daily	7-10 days	High-dose amoxicillin is used for coverage of drug-resistant *S. pneumoniae* (DRSP). Risk factors for DRSP include age > 65 years, beta-lactam therapy within past 3 months, alcoholism, multiple medical comorbidities, and exposure to a child in a day care centre. For aspiration pneumonia, Amoxicillin-clavulanate (or other BLBLIs) is recommended for anaerobic coverage. If levofloxacin is used, metronidazole should be added (oral 400mg three times daily).
Amoxicillin-clavulanate or other BLBLIs# (oral)	1g (875 mg /125 mg) twice daily	7-10 days	
Doxycycline (oral)	100 mg twice daily	7-10 days	As a combination treatment with beta-lactams for atypical pneumonia coverage. Initial empirical therapy that covers *M. pneumoniae* is considered optional for outpatients with mild CAP.
Second line			
Ceftriaxone (IV or IM)	1-2g/day in 1 to 2 divided doses (maximum: 4000 mg per day)	7-10 days	For failed initial therapy, ill presentation, non-type 1 penicillin allergy. Daily doses greater than 2g are divided into 2 doses.
Levofloxacin (oral)†	500 mg once daily	7-10 days	For outpatients who have failed the first line agent, or are allergic to the first line agent, or have documented infection by *S. pneumoniae* resistant to penicillin.

Version: November 2018 -







Pneumonia acquired outside hospital and within first 48 hours of admission

Bacteria:

- *Streptococcus pneumoniae, Moraxella catarrhalis*
- Group A strep and *Staphylococcus aureus* (post-viral)
- *Mycoplasma pneumoniae*

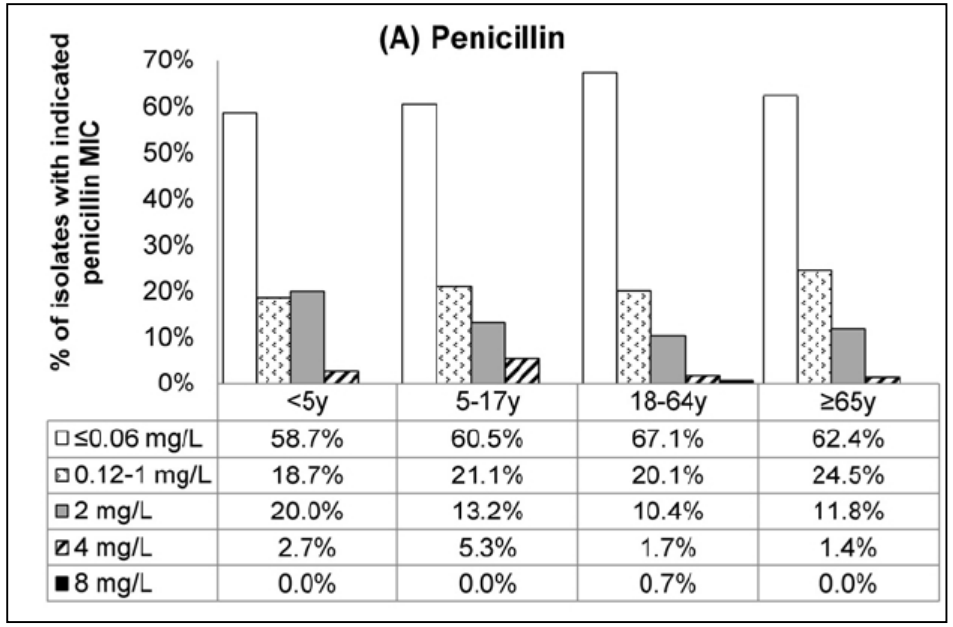
Treat with typical & atypical coverage except for mild cases

STREPTOCOCCUS PNEUMONIAE

Higher dose may be needed if risk factors for resistance present:

- >65 years old
- Beta lactam use in past 3 months
- Medical comorbidities
- Exposed to child in daycare centre
- Lack of immunization with pneumococcal conjugate vaccine

Most oral cephalosporins do not provide reliable coverage at present



	<5y	5-17y	18-64y	≥65y
≤0.06 mg/L	58.7%	60.5%	67.1%	62.4%
0.12-1 mg/L	18.7%	21.1%	20.1%	24.5%
2 mg/L	20.0%	13.2%	10.4%	11.8%
4 mg/L	2.7%	5.3%	1.7%	1.4%
8 mg/L	0.0%	0.0%	0.7%	0.0%

Susceptibility of 775 invasive pneumococcal isolates to penicillin and cefotaxime according to patient age groups, 2012–2016, HK (Source: IMPACT 5thEdition)

Throat swab specimens													
Organism	**Drugs**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Beta-haemolytic streptococcus of Lancefield Group A, C & G	Penicillin	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	
	Erythromycin	37%	100%	43%	67%	40%	75%	60%	29%	100%	50%	100%	
No. of isolates		19	1	7	3	5	4	5	7	3	4	5	

Sputum specimens													
Organism	**Drugs / Resistance phenotype**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Streptococcus pneumoniae	Penicillin	13%	29%	15%	16%	25%	27%	18%	29%	29%	43%	13%	
	Erythromycin	60%	79%	81%	80%	79%	82%	94%	71%	71%	86%	63%	
	Levofloxacin	13%	4%	4%	8%	0%	0%	0%	0%	0%	14%	6%	
No. of isolates		15	24	26	25	24	11	17	7	7	7	16	
Haemophilus influenzae	Ampicillin	46%	47%	44%	48%	49%	48%	42%	61%	43%	42%	39%	
	Amoxicillin + clavulanic acid	11%	16%	15%	16%	14%	15%	11%	21%	16%	14%	12%	
No. of isolates		157	154	292	246	287	131	132	112	88	88	85	
Moraxella catarrhalis	BL+	97%	93%	99%	97%	99%	100%	100%	100%	96%	100%	99%	
No. of isolates		239	144	89	70	90	53	57	35	26	72	100	

Bacterial pathogen isolation and percentage of antimicrobial resistance, out-patient setting, 2018 (data from CHP)

Detection of Mycoplasma pneumoniae in respiratory specimens in 2018

Testing for Mycoplasma pneumoniae is generally undertaken for specimens of respiratory secretions from patients with clinical diagnosis of community-acquired pneumonia.

Month	No. tested	No. positive	% positive	Macrolide resistance (A2063G in 23S rRNA gene)		
				No. tested	No. detected	%
January	657	15	2.3	15	2	13.3
February	673	5	0.7	5	1	20.0
March	674	8	1.2	8	2	25.0
April	606	8	1.3	8	1	12.5
May	567	17	3.0	17	7	41.2
June	499	9	1.8	9	5	55.6
July	597	13	2.2	13	5	38.5
August	581	15	2.6	15	4	26.7
September	508	11	2.2	11	4	36.4
October	649	10	1.5	10	1	10.0
November	651	21	3.2	21	6	28.6
December						

Table 2. Antibiotic recommendation for treatment of Community-Acquired Pneumonia in children -

Drug (Route)	Dosage and Frequency, Children^ (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin (oral)	45 mg/kg/day or 90 mg/kg/day (maximum: 3000 mg/day) in divided doses every 8 or 12 hours	7-10 days	In outpatients without risk factors for DRSP, amoxicillin dosing of 45 mg/kg/day may be used. In outpatients with risk factors for DRSP, amoxicillin dosing of 90 mg/kg/day is required. Risk factor for DRSP: antibiotic consumption in recent 3 months. Choose the preparation that could provide the required amoxicillin dose with the least amount of clavulanate to reduce side effects e.g. diarrhea
Amoxicillin-clavulanate or other BLBLIs# (oral)	45 mg/kg/day or 90 mg/kg/day of the amoxicillin component (maximum: 3000 mg/day) in divided doses every 12 hours	7-10 days	
Azithromycin or other macrolides e.g. clarithromycin (oral)	For children <15 kg (<3 years): 10 mg/kg once daily For children ≥ 15 kg: 15-25 kg (3-7 years): 200 mg once daily; 26-35 kg (8-11 years): 300 mg once daily; 36-45 kg(12-14 years): 400 mg once daily; Over 45 kg: Dose as per adults	3-5 days	As a combination treatment with beta-lactams for atypical pneumonia coverage. Initial empirical therapy that covers M. pneumoniae § is considered optional for outpatients with mild CAP. It may be indicated if the patients have severe CAP or are children ≥ 5 years and adolescents.
Second line			
Ceftriaxone (IV or IM)	50 to 100 mg/kg/ day IV or IM in divided doses every 12 or 24 hours (maximum: 4000 mg per day)	7-10 days	For failed initial therapy, ill presentation, non-type 1 penicillin allergy. Daily doses greater than 2g are divided into 2 doses.
Cefpodoxime (oral)	Infants >3 months of age and Children <12 years of age: Oral: 5 mg/kg/dose (maximum: 200 mg/dose) every 12 hours Children ≥12 years of age and Adolescents: refer to adult dosing	7-10 days	For non-type 1 penicillin allergy. Certain *S. pneumoniae* isolates may not be reliably covered by oral cephalosporins in the local setting.
Cefuroxime (oral)	Infants >3 months of age and Children <40 kg: 15 mg/kg/dose (maximum : 250 mg/dose) every 12 hours; Children ≥40 kg: maximum: 500 mg/dose every 12 hours	7-10 days	
Clindamycin@ (oral)	30 to 40 mg/kg/day in divided doses every 6 to 8 hours	7-10 days	For empirical treatment of suspected pneumococcal pneumonia with severe (type 1) allergy to penicillin (rare). Certain *S. pneumoniae* isolates may not be reliably covered by oral clindamycin in the local setting.

^ Dosages listed are not appropriate for neonates.
§ Doxycycline is recommended for the treatment of macrolide-resistant *M. pneumoniae* (MRMP) associated CAP in children > 8 years old, adolescents and adults.
Doxycycline may be given orally at 2 mg/kg (maximum: 100 mg) twice daily.
† Beware of possible serious side effects (e.g. joint or tendon pain, muscle weakness, tingling or pricking sensation, numbness in the arms or legs, confusion, and hallucinations).
# Beta-lactam-beta-lactamase inhibitor combinations e.g. ampicillin-sulbactam.
@Only capsule (not syrup) preparation is available locally. The capsule is dosed as 150mg each.
Clinicians should tailor make drug treatment based on clinical judgment. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available.
Management of outpatients with infections should be individualised. Doctors should check, document and get outpatients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.).
Outpatients should be reminded to take antibiotics exactly as prescribed by their family doctors.

Antibiotic Stewardship Programme in Primary Care Guidance Notes
Acute Exacerbations of Chronic Obstructive Pulmonary Disease

1. Acute exacerbations of COPD can be precipitated by several factors. The most common causes are respiratory tract infections.

2. Usual causative pathogens include *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae*. In advanced COPD, *Pseudomonas aeruginosa* and Enterobacteriaceae may cause infections.

3. In the outpatient settings, antibiotics should be given to patients
   (a) following three cardinal symptoms:
   - increased dyspnoea
   - increased sputum volume
   - increased sputum purulence

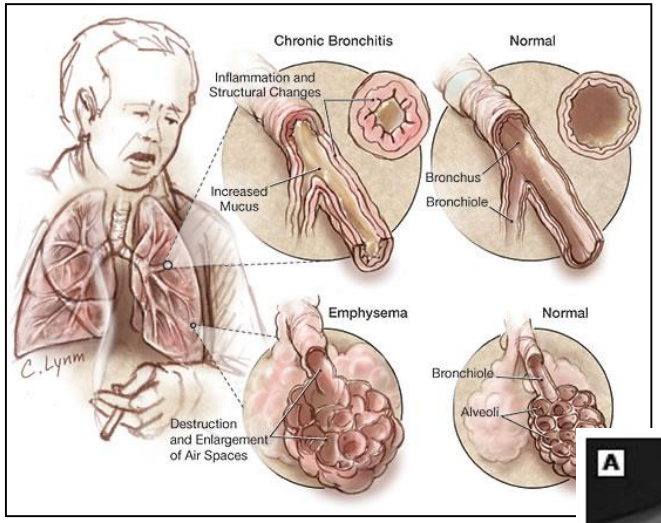
   or

   (b) with increased sputum purulence and one other cardinal symptom.

4. Amoxicillin-clavulanate, instead of amoxicillin, is recommended as the former is active against beta-lactamase-producing bacterial pathogens commonly encountered in such infections.

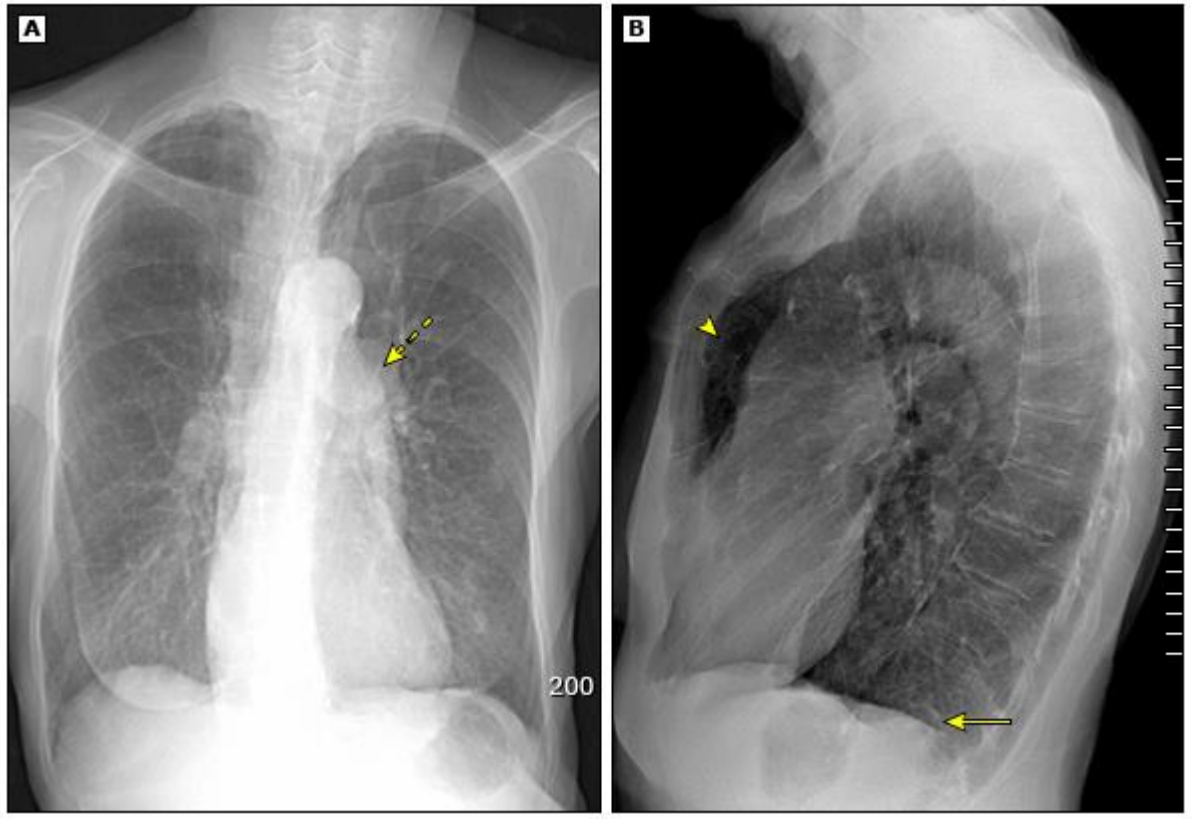
5. Fluoroquinolones may be considered when *P. aeruginosa* infection is suspected. However, due to concern for serious side effects involving tendons, muscles, joints, nerves and the central nervous system, they should be used to treat acute exacerbations of chronic bronchitis only if there are no alternative options.

Version: November 2018 -



JAMA

Chronic exposure to harmful chemicals e.g. tobacco smoking causing alveolar abnormalities



CXR of flattened diaphragm & hyperinflation in COPD patient

Uptodate

ACUTE EXACERBATION OF COPD

Acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication

Triggers: infections, air pollution, change in temperature, pulmonary embolism

Typical symptoms:

- Cough frequency and severity ⇧
- Sputum volume ⇧ and/or change in character
- Dyspnea ⇧

ANTIBIOTIC FOR AECOPD

GOLD recommends antibiotics use in :

- All 3 cardinal symptoms
  - Increased sputum purulence
  - Increased sputum volume
  - Increased dyspnea
- Increased sputum purulence with one other cardinal symptoms
- Severe cases requiring mechanical ventilation (hospitalization?)

Global Strategy for the Diagnosis, Management and Prevention of COPD 2018

Many pathogens associated with AECOPD produce beta-lactamases

Risk factors for *Pseudomonas*: Frequent admission to hospital and antibiotics, previous positive culture, use of systemic steroid

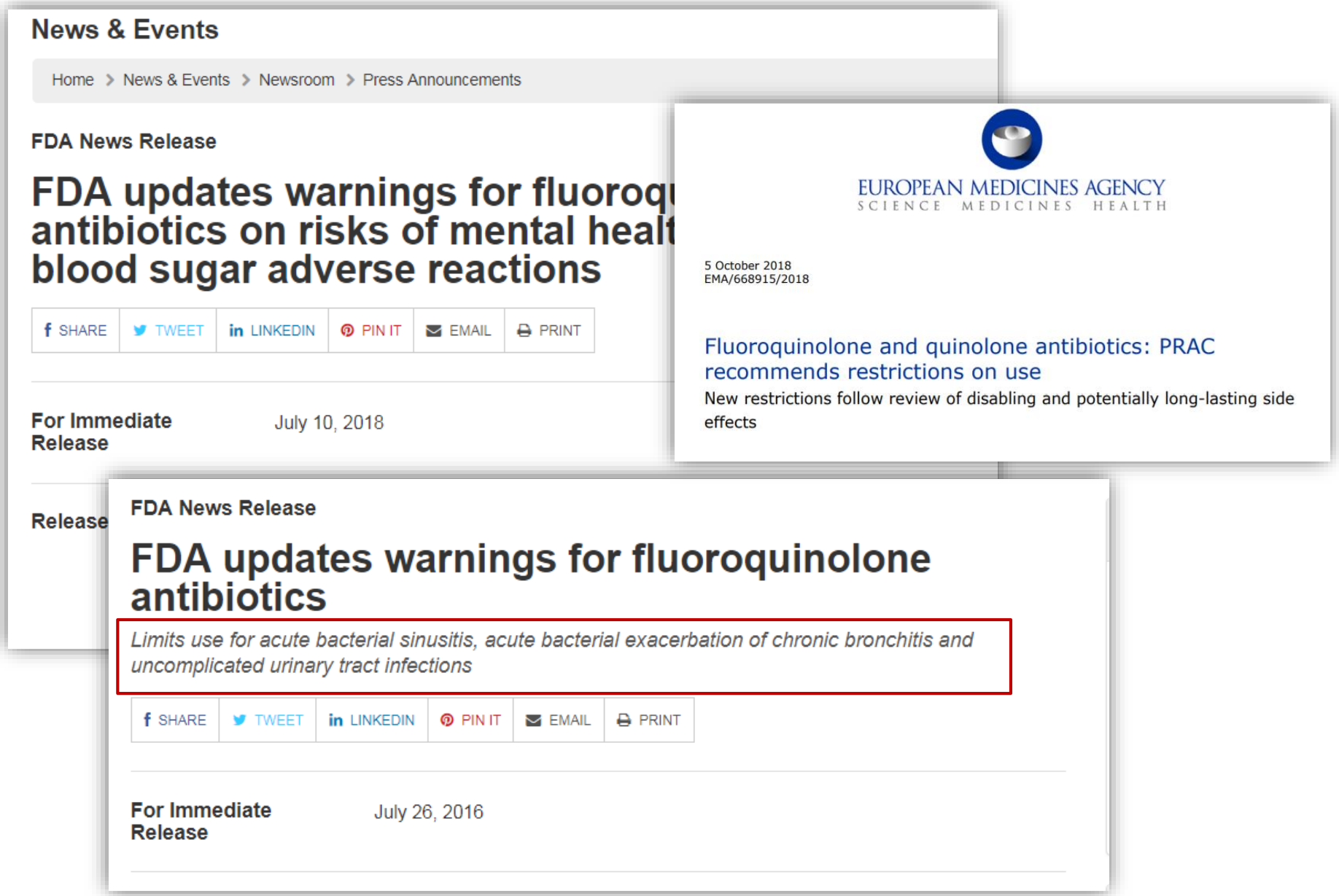
Table 1. Antibiotic recommendation for treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease* -

Drug (Route)	Dosage and Frequency, Adults (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin-clavulanate or other BLBLIs# (oral)	1g (875 mg /125 mg) twice daily; or 625mg (500 mg/125mg) three times daily	5-7 days	Amoxicillin-clavulanate is active against beta-lactamase-producing organisms (e.g. *H. influenzae*, *M. catarrhalis* and methicillin-sensitive *Staphylococcus aureus*).
Second line			
Ceftriaxone (IV or IM)	50 to 100 mg/kg/ day IV or IM in 1 to 2 divided doses (maximum: 4000mg per day)	5-7 days	For non-type 1 penicillin allergy. Daily doses greater than 2g are divided into 2 doses.
Cefpodoxime (oral)	200 mg twice daily	7-10 days -	For non-type 1 penicillin allergy. Certain *S. pneumoniae* isolates may not be reliably covered by oral cephalosporins in the local setting.
Levofloxacin† (oral)	500 mg once daily	7-10 days	For outpatients who have either: -Failed the first line agent, or -Allergy (including type-1) to the first line agent, or -Documented infection by *S. pneumoniae* resistant to penicillin, or -Suspected *P. aeruginosa* infection.
Moxifloxacin† (oral)	400 mg once daily	5-10 days	

Beta-lactam-beta-lactamase inhibitor combinations e.g. ampicillin-sulbactam.

† Fluoroquinolones should be reserved for use in outpatients who have no other treatment options

Clinicians should tailor-make drug treatment based on clinical judgment. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available. Management of outpatients with infections should be individualised. Doctors should check, document and get outpatients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.). Outpatients should be reminded to take antibiotics exactly as prescribed by their family doctors.



- Risk factors for tendonopathy:
  - Elderly
  - Chronic Renal failure
  - Concomitant steroid

- Indicated: according to susceptibility results, beta-lactam allergies, failed first-line therapy

PUBLICITY

Meeting Highlights and CME Calendar

The HKMA Central, Western and Southern Community Network (CW&SCN) ~ Dr. YIK Ping Yin

Group photo taken during the lecture on 20 February 2019 From left: Dr. YIK Ping Yin, Dr. Francis WONG (speaker) and Dr. TSANG Chun Au (moderator)

The HKMA Kowloon East Community Network (KECN) ~ Dr. AU Ka Kui, Gary

Dr. Jennifer CHU (left, moderator) and Dr. CHEUNG Ling Ling (speaker) in photo during the lecture on 21 February 2019

The HKMA New Territories West Community Network (NTWCN) ~ Dr. CHEUNG Kwok Wai, Alvin

Group photo taken during the lecture on 21 February 2019 From left: Dr. TSUI Fung, Dr. Eddy LAM (speaker) and Dr. Alvin CHEUNG (moderator)

The HKMA Kowloon West Community Network (KWCN) ~ Dr. TONG Kai Sing

Dr. Leo LUI (left, speaker) and Dr. MOK Kwan Yeung (moderator) in photo during the lecture on 26 February 2019

The HKMA Yau Tsim Mong Community Network (YTMCN) ~ Dr. CHENG Kai Chi

Dr. Carmen HO (left, moderator) and Dr. Leo LUI (speaker) in photo during the lecture on 19 February 2019

The HKMA Hong Kong East Community Network (HKECN) ~ Dr. CHAN Nim Tak, Douglas

Dr. Kenneth YIP (right, moderator) presenting a Certificate of Appreciation to Dr. Florence LEE (speaker) during the lecture on 21 February 2019

The HKMA Kowloon City Community Network (KCCN) ~ Dr. CHIN Chu Wah and Dr. CHAN Man Chung, JP

Dr. Leo LUI (right, speaker) and Dr. CHAN Man Chung, JP (moderator) in photo during the lecture on 22 February 2019


pdate on Antibiotic
ardship Programme
P) in Primary Care
Dr Leo Lui
Consultant
ntrol Branch
th Protection


THE END

Communicable Diseases WATCH

EDITORIAL BOARD Editor-in-Chief Dr SK Chuang Members Dr Yonnie Lam / Dr Albert Au / Dr TY Wong / Dr Gladys Yeung / Dr Philip Wong / KK So / Sheree Chong / Doris Choi / Chloe Poon Production Assistant Yoyo Chu. This biweekly publication is produced by the Centre for Health Protection (CHP) of the Department of Health, 147C,Argyle Street, Kowloon, Hong Kong ISSN 1818-4111 Please send enquiries to cdssinfo@dh.gov.hk.

FEATURE IN FOCUS

New series of Guidance Notes on Antibiotic Stewardship in Primary Care

Reported by Dr Leo LUI, Associate Consultant, Infection Control Branch, CHP.

Antimicrobial resistance (AMR) is a global public health problem. For the past few decades, AMR has been a growing threat to effective treatment for an ever-increasing number of infections caused by bacteria, viruses, fungi and parasites. AMR results in reduced efficacy of antimicrobials, making the treatment of patients difficult, costly or even impossible, causing prolonged course of illness and increased disease mortality.

In July 2017, the Government of the Hong Kong Special Administrative Region (HKSAR) launched the Hong Kong Strategy and Action Plan on Antimicrobial Resistance (2017-2022). It adopted the "One Health" approach as recommended by international health agencies such as the World Health Organization, as a holistic model with a view to curb the growing threat of AMR in Hong Kong. Among the different aspects of the One Health approach, one of the key areas is to optimise the use of antimicrobials in the healthcare settings.

Antibiotic Stewardship Programme (ASP) is identified as a key measure for improving patient outcomes by reducing unnecessary prescriptions, and when they are genuinely needed, ensuring these important drugs are used at a proper dose and the duration is kept to be as short as necessary without compromising patient safety. A successful ASP has many potential benefits, including delaying the emergence of resistant micro-organisms, minimising adverse effects of antimicrobials and their administration, reducing length of hospital stay and thus the incidence of healthcare-associated infections, and finally often a reduction of the cost of antimicrobials. Broadly speaking, ASP can be implemented in almost all healthcare settings, including both in- and out-patient facilities. There are different ways of delivering an ASP model, one important means is through provision of professional guidance in an easily-accessible and user-friendly manner.

The Centre for Health Protection (CHP) of the Department of Health launched the Antibiotic Stewardship Programme in Primary Care (ASP in PC) in November 2017. Evidence-based Guidance Notes (GNs) for common infections diagnosed by primary care doctors (such as acute pharyngitis, acute uncomplicated cystitis in women and simple (uncomplicated) skin and soft tissue infections) were developed. Health education materials including patient information sheets, posters, pamphlets and tips for taking antibiotic cue cards were also made available to assist primary care doctors to explain to patients the nature of diseases and the importance of compliance with doctors' instructions when patients were prescribed with an antibiotic. The GNs were then promulgated through Continuing Medical Education ("CME") seminars to primary care doctors.

The Infection Control Branch (ICB) of CHP organised nine briefing sessions of ASP in PC from December 2017 to March 2018 for medical doctors in Hong Kong. A questionnaire survey was conducted to over 400 participants. Results showed that GNs were considered useful and had strong influence on doctors' decision in antibiotic prescription.

With positive feedback from primary care doctors, the Advisory Group on ASP in PC continued to develop the second series of GNs (Figure 1) on common infections seen by primary care doctors. There are four conditions focusing on the upper respiratory tract and lower respiratory tract conditions in the new set of guidance notes. The topics are: 1) acute otitis media, 2) acute rhinosinusitis, 3) community-acquired pneumonia, and 4) acute exacerbations of chronic obstructive pulmonary disease. In each guidance note, the indications of when to prescribe antibiotics, choices of appropriate agents, dose and duration of antibiotics are recommended based on the best available clinical evidence with a perspective of local practices. Each guidance note is presented in a long and short version, with the long version serving to explain the rationale of recommendations in details while the short versions (in the form of A5-sized quick reference guides) are intended to be used conveniently by primary care doctors at the point of care during or in between patient consultations.

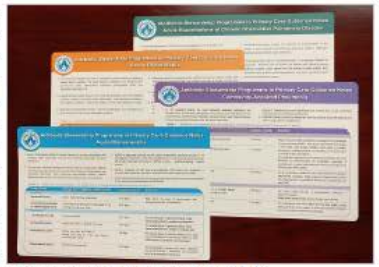


Figure 1 - The second series of Guidance Notes.

As in the previous round, patient information sheets are also prepared to facilitate doctors to teach patients how to properly use antibiotics and to understand more about their course of illness in general. Electronic copies of the guidance notes are being uploaded onto the webpage of ASP in PC (https://www.chp.gov.hk/en/features/49811.html) (Figure 2).

Figure 2 - The webpage of Antibiotic Stewardship Programme in Primary Care.

Hard copies will be distributed to individual primary care doctors, medical groups, private hospitals and other doctors as necessary. Recommended practices will also be promulgated through CME seminars to primary care doctors in Q4 of 2018 and Q1 of 2019. For the first time ever, these seminars will be broadcasted live through CME-approved online video streaming platforms viewable by primary care doctors who are unable to attend the seminar in person but are enrolled with the CME programme.

HPV Vaccination for Cervical Cancer Prevention

Reported by Dr HO King-man, Head of Public Health Services Branch, CHP.

Human Papillomavirus (HPV) is a small non-enveloped double stranded DNA virus. There are more than 200 types of papillomavirus, of which around 40 infect human mucosal areas including the anogenital tract. The 40 HPVs are divided into high risk and low risk HPV (HR-HPV and LR-HPV respectively) according to their oncogenic potential. Persistent infection of the HR-HPVs may cause cancer of the infected mucosae. In local studies, HPV-16 and HPV-18 are the most commonly identified HR-HPVs in cervical cancer specimens and together they accounted for about 70% of cervical cancer. HR-HPV type 52, 58, 33, 31 and 45 in descending order of occurrence are the other HPV identified in another 20% of cervical cancer specimens[1,2,3]. Whereas HPV-6 and HPV-11 are the commonest low-risk HPVs (LR-HPV) that cause anogenital warts.

Transmission of genital HPV infection is mainly through sexual contact (both vaginal and anal sex) with an infected person. Primary prevention of cervical cancer involves behavioural modification including safer sex with condom usage, reducing number of sexual partners, avoidance of smoking and vaccination against HR-HPVs. Secondary prevention involves cervical screening to identify and treat precursor lesions of invasive cervical cancer. A territory wide cervical screening programme has been launched in Hong Kong since 2004 to reduce the local cervical cancer burden.

Antibiotic management of acute pharyngitis in primary care

The Advisory Group on Antibiotic Stewardship Programme in Primary Care

ABSTRACT

The Centre for Health Protection of the Department of Health has convened the Advisory Group on Antibiotic Stewardship Programme in Primary Care (the Advisory Group) to formulate guidance notes and strategies for optimising judicious use of antibiotics and enhancing the Antibiotic Stewardship Programme in Primary Care. Acute pharyngitis is one of the most common conditions among out-patients in primary care in Hong Kong. Practical recommendations on the diagnosis and antibiotic treatment of acute streptococcal pharyngitis are made by the Advisory Group based on the best available clinical evidence, local prevalence of pathogens and associated antibiotic susceptibility profiles, and common local practice.

Hong Kong Med J 2019;25:58–63
https://doi.org/10.12809/hkmj187544

The Advisory Group on Antibiotic Stewardship Programme in Primary Care

(Group members are listed at the end of the paper)

Corresponding author: edmanlam@cuhk.edu.hk

This article was published on 31 Jan 2019 at www.hkmj.org.

Introduction

The Government of the Hong Kong Special Administrative Region attaches great importance to the threat of antimicrobial resistance. Under the authority of the Food and Health Bureau, and with collaborative efforts from stakeholders, the Hong Kong Strategy and Action Plan on Antimicrobial Resistance (2017-2022) was established in July 2017. Recommendations in six key areas and 19 objectives were included in this Action Plan, aiming to slow the antimicrobial resistance containment measures by not only practising rational antibiotic prescriptions but also educating and engaging out-patients about the safe use of antibiotics during clinical encounters.

Acute pharyngitis is the acute inflammation of the oropharynx. It is characterised by sore throat and pharyngeal erythema. It is one of the most common conditions among out-patients in primary care in Hong Kong.[1,2]

Acute pharyngitis is usually a benign, self-

Self Study CME Series No.211 (1 CME Point)

Management of Antibiotic Allergy in the Era of Antimicrobial Resistance

Allergy to antibiotics is a commonly encountered condition. This article will briefly discuss on aspects including classification, prevalence, diagnosis and recommended approach in primary care setting.

Classification of antibiotic allergy

There are 4 types of allergic reactions in classical teaching. For practical purpose, we can classify them into type 1 (acute) and non-type-1 (delayed) reactions. Type-1 reactions are mediated by IgE antibodies with a fast onset typically within 1 hour. Hallmark features are urticaria, wheezing, angioedema and anaphylaxis. This is the type of reaction that skin test aims to exclude. Delayed reactions are mediated by other immune mechanisms with a more gradual and variable onset (1-2 days to weeks). Manifestations can be diverse, ranging from mild skin rash to systemic upset like fever, eosinophilia, cytopenia, liver and renal impairment. Except for certain severe delayed reactions such as Steven Johnson Syndrome, hemolysis and acute interstitial nephritis, delayed reactions are not contraindications to further use with care. Certain side effects of antibiotics e.g. headache, GI upset and dizziness are not true allergy and should not be labelled as such. In paediatrics, most skin rashes are due to viral-drug interaction (as in infectious mononucleosis) which do not indicate true allergy. Some antibiotics e.g. vancomycin, amphotericin B may also produce infusion reactions mimicking systemic allergy reactions.

Epidemiology of penicillin allergy

Among all antibiotics, penicillin is the most commonly reported drug to cause allergy. Overseas data show that 10% of the general population have allergy labels, although less than 1% are truly allergic (IgE-mediated). Overall, 80-90% of them eventually can tolerate penicillin treatment. The prevalence of penicillin allergy is falling because of purer penicillin preparations nowadays, and decreased use of intramuscular injections. For any individual, the likelihood of reaction drops by about 10% per year on average, so that most would have lost their reactions in 10 years. The prevalence of anaphylaxis is quoted to be 0.02-0.04% and is also decreasing. Cross-reactivity between penicillins and cephalosporins depend on similarity of their side chains. The frequently quoted figure of 10% cross-reactivity rate is likely an overestimate from contaminated penicillins in the past. Recent systematic review has found that the rate is usually <5% with

low-risk individuals can usually skip skin test and proceed directly to graded oral drug challenge (DC). DC is performed usually with amoxicillin. Patients are observed for 30 to 60 minutes after the challenge dose (1/10th of full dose) is given. If uneventful, the full dose is given followed by another observation. Although acute reactions are excluded by a negative DC, benign delayed reactions can still develop several days later in about 3% of patients, which is the rate observed in general population.

Effect of penicillin allergy on patient and society

Beta-lactams are considered as the drug of choice for many common or severe infections, such as beta-hemolytic streptococci, staphylococci, listeriosis, gonorrhea and syphilis. Penicillin allergy is associated with adverse patient outcomes, including longer hospital stay, higher rate of infection by resistant organisms e.g. C. difficile, MRSA & VRE, increased adverse effects from the use of alternative antibiotics. Surgical prophylaxis with non-beta-lactam regimen leads to an increased risk of surgical site infection. Significantly higher healthcare cost is noted among penicillin-allergic subjects.

Allergy and Antibiotic Stewardship Programme (ASP)

Evaluation of allergy should be part of ASP. The objective is to maximize the prescription of first-line beta-lactam agents whenever indicated. There is an increasing amount of literature reports highlighting efforts to integrate evaluation by means of history-taking, PST and DC into various ASPs in in-patient and out-patient settings. Many patients were successfully "delabelled" after proper assessment by doctors, nurses or pharmacists. Cost-effectiveness and enhanced use of beta lactams without increase in adverse reactions have been demonstrated.

Suggested approach in Primary Care

After detailed history taking, an 'allergic' patient may be classified into one of the 3 categories: high risk (acute or severe delayed reactions) / low risk (benign delayed reactions) / non-allergy. For the low-risk category, direct DC with amoxicillin may be attempted. The rate of serious reactions or death after DC reported in the literature is extremely low. Ambulatory facilities are considered as ideal settings for DC because patients are usually not very ill without an urgent need of antibiotics. Nevertheless, standard antianaphylaxis medications should be

SELF STUDY CME SERIES

Summary

1. Type-1 (acute) reactions have a rapid onset typically within 1 hour. It is marked by urticaria, wheezing, angioedema and anaphylaxis. Severe delayed reactions include Steven Johnson Syndrome, hemolysis, organ dysfunction, etc. Both types of reactions are considered absolute contraindications to reuse of the implicated antibiotic.
2. Penicillin is the most common antibiotic associated with allergy. About 10% of the population are reported as penicillin-allergic, but <1% have true allergy (type-1 reactions).
3. History taking is the most important step in diagnosing antibiotic allergy. We should ask about the circumstances of the exposure episode, characteristics of the symptoms, prior evaluation results and name of the tolerated agents.
4. Penicillin allergy is associated with adverse patient outcomes e.g. longer length of hospital stay and infections with resistant microorganisms. Antibiotic Stewardship Programme (ASP) should include allergy assessment to facilitate use of first-line beta lactam antibiotics whenever indicated.
5. In primary care setting, graded oral antibiotic challenge may be attempted for patients without features of type-1 (acute) or severe delayed reactions. 30 to 60-minute observation should follow each dose administered. Antianaphylaxis medications should be readily available.

Questions

1. Which of the following is not a typical sign and symptom of type-1 (acute) reaction?

A. Urticaria
B. Angioedema
C. Wheezing
D. Anaphylaxis
E. Pruritis without rash

2. About ___% of general population is reported to be allergic to penicillin.

A. 1
B. 5
C. 10
D. 20
E. 30

3. Which of the following statement is incorrect?

A. Cross reactivity between penicillin and cephalosporins are determined by similarity of side chains
B. 3rd and 4th generation cephalosporins have very low cross-reactivity rate with penicillin

4. Penicillin allergy is associated with the following adverse outcomes except:

A. Longer hospital stay
B. Increased risk of infection by drug-resistant organisms e.g. C. difficile, MRSA, VRE
C. Higher healthcare cost
D. Increased risk of surgical site infection
E. Higher risk of tendonopathy

5. Which of the following statements about graded drug challenge (DC) is true?

A. The minimal number of doses is 3 (1/100th, 1/10th, full dose)
B. An observation period of 4 hours is required after administering the challenge doses
C. Test is commonly performed using oral amoxicillin
D. Negative result can effectively rule out all types of allergic reaction
E. Can only be performed in allergy specialist clinics

Date of writing: 13th May 2020

Self Study CME Series No.217 (1 CME Point)

Rational Use of Antibiotics in COVID-19 Pandemic

Ongoing battle against antimicrobial resistance (AMR) with limited supply of antibiotics

COVID-19 hits us in all walks of life. While we concentrate on finding a cure and vaccine for this novel infection, it is equally important that we do not lose sight on rational use of antibiotics[1]. Antibiotics are lifesaving for patients with cancer, dialysis, surgery, and many other treatment procedures. Prior to COVID-19, 700,000 deaths annually worldwide were caused by infection with drug-resistant organisms[2], which is almost three times the toll of COVID-19 so far; up to half of surgical site infections in developed countries are caused by drug-resistant microorganisms[3]. If no action is taken, mortality has been projected to 10 million per year by 2050 with economic loss comparable to the 2008 global financial crisis[4]. The pipeline of antibiotics has been dry due to the upside-down economics for antibiotic development: the less drugs people take, the better they work[5]. Five companies that brought new agents to market in past 3 years have gone bankrupt or left the field[2]. More than half of the new drugs in development are still in Phase 1 or 2 trials, taking them years for approval[6]. None of the candidates for treating the WHO-critical-threat pathogens is based on novel mechanism to safeguard against resistance development[7].

What is rational use of antibiotics?

We cannot just wait for new antibiotics to do our work. We need to continue practicing rational use of antibiotics to preserve their activities against targeted bacteria. Rational use means giving the right drug at the right time and right dose, for the right duration[8]; prescribe only as indicated and keep the course as short as possible. Benefits of responsible prescription includes fewer side effects for the patient, lower chance of emergence of resistance and reduced clinical workload in administering parenteral infusions[1]. Rational use is especially important at times when global supply of specific antibiotics may be disrupted due to shortages of raw materials and active pharmaceutical ingredients[2]. During COVID-19 pandemic, antibiotics should be viewed as crucial as masks and other personal protective equipment (PPE)[9].

Co-infections in viral pandemics

In a viral pandemic, antibiotics are mostly used to treat secondary bacterial infections. It is known that after influenza, *Streptococcus pneumoniae and Staphylococcus aureus* can cause secondary infections in about 35% and 28% respectively[10]. Other less common microbes include *Haemophilus influenzae, Streptococcus pyogenes, Pseudomonas aeruginosa* and fungi e.g. *Aspergillus*[10,11]. In fact, the vast majority of some 100 million deaths in the 1918 Spanish influenza was caused not by the virus itself but by secondary bacterial pneumonia[12]. Similarly, swine influenza (H1N1) in 2009 had up to 55% secondary infection rate[13] among the estimated deaths of 284,000[14].

SARS-CoV-2 and other pathogens are urgently required[15].

Characteristics of antibiotic use in COVID-19 patients

COVID-19 has caused a huge number of old and frail to be admitted to hospitals. The threshold of antibiotics for these patients is low because of high risk of deterioration. Covering the infection with empirical antibiotics is justified in initial phase as differentiation between viral and bacterial pneumonia is difficult, but the antibiotics prescription rate for COVID-19 patients appears exceedingly high at about 72%-95%[16,17]. One reason could be the overwhelming anxiety from the pandemic and the absence of antiviral treatment with proven efficacy[1]. Furthermore, diagnostic procedures that generate aerosols e.g. bronchoscopy and open suctioning of airways may be less frequently performed due to concerns in infection control e.g. PPE shortage, decreasing the number of microbiological sampling to guide targeted antimicrobial treatment.

In finding a cure, many drugs have been investigated as treatment of COVID-19, some of them are antimicrobials. For example, azithromycin (in conjunction with hydroxychloroquine, an anti-malarial drug) was previously advocated in France[20], while tetracycline, doxycycline[21] and even teicoplanin[22] have also been suggested. But none of these agents is currently considered standard of therapy[23]. Of note, political factors can affect the use of antibiotics, for example, support of azithromycin by Donald Trump has caused a shortage of azithromycin in the U.S.[24]

How should antibiotics be prescribed in the context of COVID-19?

We can keep the following principles in mind when we use antimicrobials in the current pandemic[1, 25, 26]:

1. Reserve antibiotics for more severe cases
2. Select empirical antibiotics according to clinical conditions e.g. indications and risk factors for resistant bacteria
3. Review the need of antibiotics after 48-72 hours
4. Obtain microbiological sample as far as possible prior to starting treatment
5. Consider intravenous to oral switch for cases with clinical improvement, if a suitable agent is available
6. Avoid empirical use of fluoroquinolones and macrolides for risk of QT prolongation, especially when the rate of atypical pneumonia appears to be low
7. Stop antibiotics after COVID-19 status is confirmed, if no definite evidence of bacterial infection is present and clinically stable
8. Consider non-infective causes of secondary worsening relevant to COVID-19, e.g. myocarditis, cytokine release syndrome

HKDU Bulletin

SELF STUDY CME SERIES

Conclusion

Amidst a highly infectious pandemic, the importance of rational use of antibiotics can be easily overlooked. While the pandemic may soon be over, the same cannot be spoken for AMR, which may in fact be exacerbated by COVID-19. Just like we need to practice our hand washing and mask wearing until a vaccine for COVID-19 is available, we need to use existing antibiotics carefully before potential game-changing novelties enter the battlefield and save the day.

Summary

1) Despite certain new antibiotics are now available in the market, their use is still limited. We need to keep prescribing antibiotics rationally as guided by antibiotic stewardship programmes.
2) Secondary bacterial pneumonia has been a well-recognized complication of influenza, but not among coronaviruses including COVID-19 according to data so far.
3) The rate of prescription of antibiotics for COVID-19 cohorts reported is remarkably high. More prudent use of antibiotics is indicated to reduce emergence of antibiotic resistance when the pandemic is over.
4) In COVID-19 pandemic, antibiotics should be reserved for more severe cases and discontinued if no definite evidence of bacterial infection in uncomplicated cases.
5) We should be cautious when using biomarkers to aid us in deciding when to start or stop antibiotics in the context of COVID-19, as their roles have not been well-defined. A similar cautious approach applies to using immunodiagnostic point-of-care tests for diagnosis.

Additional Information

Biomarkers for prediction of bacterial infection

The biomarker procalcitonin has been employed to predict bacterial infections clinically, but their utility for COVID-19 is currently uncertain. While values are low in most patients with COVID-19, they appear to rise with disease severity as part of the systemic inflammatory process regardless of secondary infections[32]. Therefore, routine testing to guide decisions on antibiotics cannot be recommended. Other biomarkers e.g. C-reactive protein (CRP) are even less predictive[29]. We should bear in mind that biomarkers are adjunctive tools. Overall clinical picture should always be considered when starting or stopping antibiotics.

Classification and limitation of rapid diagnostic test

An early diagnosis can facilitate clinical management and infection control. For a completely new infection like COVID-19, the Food and Drug Administration (FDA) would grant emergency use authorizations (EUA) to previously unapproved tests for use under specified conditions based on laboratory data, scientific literature and clinical need. At the time of writing, 68 in-vitro diagnostic tests have been granted EUA, most are laboratory-based molecular and serology tests[33]. A few of them can be used at the point of care e.g. clinics with results available in a short time frame e.g. within 1 hour, but widespread use in such setting is limited by the high cost for molecular-based tests (including film-array which is a multiplex PCR system simultaneously detecting over 20 respiratory pathogens), especially if the test volume is small, and the lower sensitivity and specificity for immunodiagnostic tests. According to World Health Organization (WHO), the latter should not be used for diagnosis of COVID-19 until more supporting evidence is available[34].

The reference list is available upon request from our secretariat at 2388 2728

Questions:

Q1 Which of the following is correct about the current scenario of antimicrobial resistance (AMR) worldwide?

A) 70000 deaths occur annually due to infection with resistant organisms
B) Mortality related to AMR is similar to that of COVID-19
C) Up to 1 in 10 surgical site infections in developed countries are caused by drug-resistant organisms
D) If no action is taken, 10 million per year can die due to AMR by 2050
E) If no action is taken, economic loss due to AMR can mount up to SARS in 2003

Q2 Which of the following is not an example of rational use of antibiotics?

A) Select empirical antibiotics according to clinical conditions as stated in guidelines
B) Review the need of antibiotics after 48-72 hours
C) Keep duration as short as possible
D) For those on parenteral antibiotics, consider switching to oral route upon clinical improvement
E) Always use the broadest spectrum of antibiotics to cover for the most resistant organisms

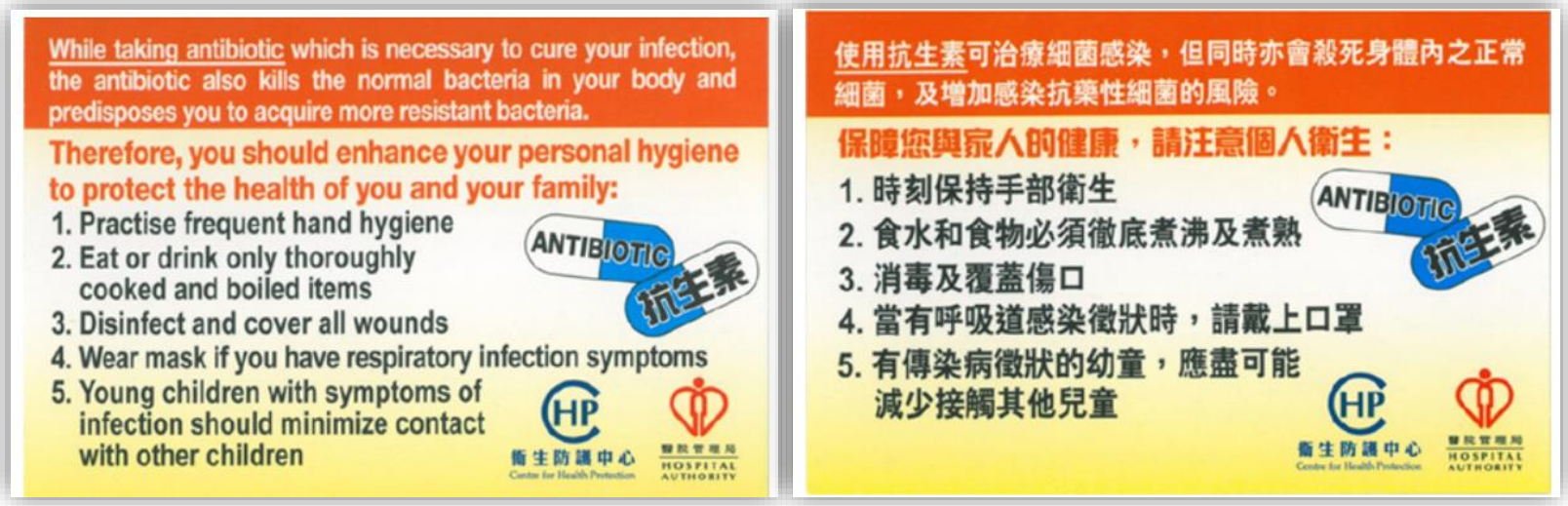
Q4 Antibiotic Stewardship team in a pandemic can help in the following ways except:

A) Update clinical management protocol related to antimicrobials
B) Identify infected cases possibly missed on admission
C) Anticipate shortage of drugs and advise pharmacy to keep adequate stocks of anti-infectives
D) Communicate critical laboratory results to clinicians
E) Perform microbiological sampling on suspected and confirmed cases

Q5 Choose the correct statement

A) A high procalcitonin level in COVID-19 is always an indication to start empirical antibiotics
B) C-reactive protein is a highly specific marker for bacterial infections
C) Polymerase chain reaction (PCR)-based tests are generally more sensitive and specific than immunodiagnostic tests
D) Emergency use authorization (EUA) is granted by the WHO for an in-vitro diagnostic test to be used clinically under emergency situations e.g. COVID-19 pandemic
E) Most diagnostics tests on the list of EUA are point-of-care tests instead of

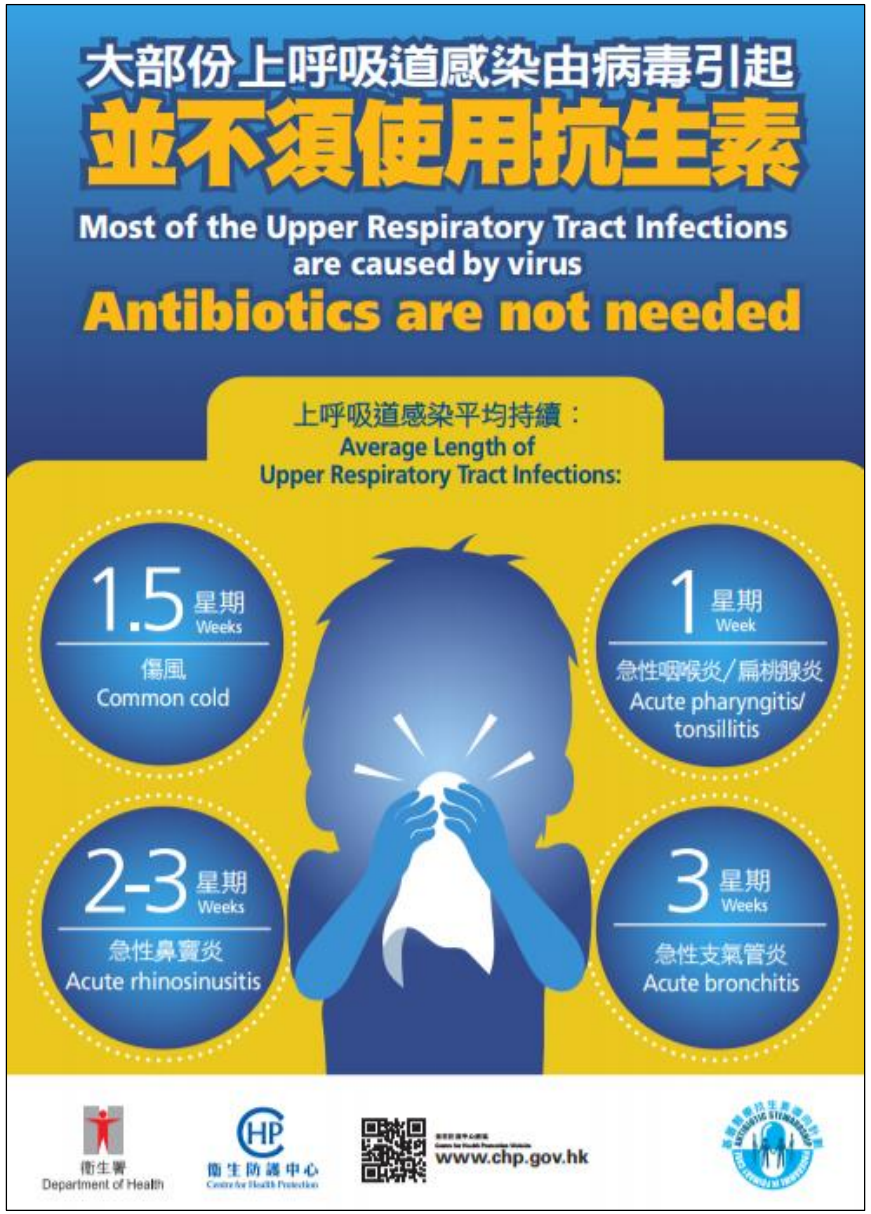
PATIENT EDUCATION MATERIALS PREPARED BY CHP



All materials are freely downloadable on CHP website
http://www.chp.gov.hk/en/view_content/49811.html

Hard copies are available upon request

Educate patients to handle antibiotics with care


大部份上呼吸道感染由病毒引起
並不須使用抗生素
Most of the Upper Respiratory Tract Infections are caused by virus
Antibiotics are not needed
上呼吸道感染平均持續：
Average Length of Upper Respiratory Tract Infections:
1.5 星期 Weeks
傷風
Common cold
1 星期 Week
急性咽喉炎/扁桃腺炎
Acute pharyngitis/ tonsillitis
2-3 星期 Weeks
急性鼻竇炎
Acute rhinosinusitis
3 星期 Weeks
急性支氣管炎
Acute bronchitis
衛生署
Department of Health
衛生防護中心
Centre for Health Protection
www.chp.gov.hk


接種流感疫苗 給孩子多一分保護
Protect your child from seasonal influenza Get flu vaccination
政府會為合資格6個月至未滿12歲（或就讀本港的小學）的兒童提供免費或資助季節性流感疫苗接種
The Government will provide free or subsidised seasonal influenza vaccination to eligible children aged between 6 months and less than 12 years (or those attending a primary school in Hong Kong)
詳情請向醫生查詢
Please consult your doctor for details
請帶同疫苗接種記錄及所需文件
Please bring along vaccination card and necessary documents
詳情 For Details
衛生防護中心網站
Centre for Health Protection Website
www.chp.gov.hk
衛生署二十四小時健康教育熱線
24-Hour Health Education Hotline of the Department of Health
2833 0111
查詢
Enquiry
2125 2125
衛生防護中心
Centre for Health Protection
疫苗接種計劃
Vaccination Schemes
衛生署
Department of Health

THANK YOU