



# Management of Group A Strep

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# Disclosures

- I have no conflicts of interest to disclose
- I will not be discussing the off-label use of any medications or devices



# Clinical care pathway at CHCO

## Uncomplicated Acute Respiratory Tract Infections (ARTI) Clinical Pathways

### ARTI clinical pathways

- [ARTI, including AOM, conjunctivitis and GAS pharyngitis](#)

<https://www.childrenscolorado.org/health-professionals/clinical-resources/clinical-pathways/uncomplicated-acute-respiratory-tract-infections/>

TM

# Who do we test for strep throat?





# Testing for GAS

**Table 3.** Accuracy for History and Physical Examination Elements in the Diagnosis of Strep Throat\*

Symptoms and Signs	Patients, No.	Accuracy	Sensitivity (95% CI) or Range	Specificity	LR+ (95% CI) or Range	LR- (95% CI) or Range
Any exudates <sup>15,16,18,19,20,21</sup>	3268	0.68	0.21-0.58	0.69-0.92	1.5-2.6	0.66-0.94
Reported fever <sup>15,17,20,21</sup>	3232	0.68	0.3-0.92	0.23-0.90	0.97-2.6	0.32-1.0
Measured temperature $>37.8^{\circ}\text{C}$ <sup>15,17,18,21</sup>	3091	0.68	0.11-0.84	0.43-0.96	1.1-3.0	0.27-0.94
Anterior cervical nodes swollen/enlarged <sup>15,16,18,20-23</sup>	3831	0.67	0.55-0.82	0.34-0.73	0.47-2.9	0.58-0.92
Pharyngeal exudates <sup>18,22,23</sup>	1673	0.65	0.03-0.48	0.76-0.99	2.1 (1.4-3.1)*	0.90 (0.75-1.1)*
Tonsillar swelling/enlargement <sup>18,19,20-22</sup>	2703	0.65	0.56-0.86	0.56-0.86	1.4-3.1	0.63 (0.56-0.72)*
Tonsillar or pharyngeal exudates <sup>15,16,19,21</sup>	2246	0.65	0.28-0.61	0.62-0.88	1.8 (1.5-2.3)*	0.74 (0.66-0.82)*
Anterior cervical nodes tender <sup>15,16,18,22</sup>	2280	0.64	0.32-0.66	0.53-0.84	1.2-1.9	0.60 (0.49-0.71)*
Tonsillar exudates <sup>20,22</sup>	840	0.64	0.36 (0.21-0.52)*	0.71-0.98	3.4 (1.8-6.0)*	0.72 (0.60-0.88)*
No cough <sup>15-19,21,23</sup>	5122	0.63	0.51-0.79	0.36-0.68	1.1-1.7	0.53-0.89
No coryza <sup>15-19,22</sup>	3846	0.57	0.42-0.84	0.20-0.70	0.86-1.6	0.51-1.4
Myalgias <sup>18,21,22</sup>	2003	0.57	0.49 (0.43-0.56)*	0.52-0.69	1.4 (1.1-1.7)*	0.93 (0.86-1.0)*
History of sore throat <sup>16,17,21,22</sup>	3090	0.57	0.18-0.93	0.09-0.86	1.0-1.1	0.55-1.2
Headache <sup>17,18,22</sup>	2350	0.56	0.48 (0.42-0.53)*	0.50-0.80	0.81-2.6	0.55-1.1
Pharynx injected <sup>16,18,19,22</sup>	2939	0.54	0.43-0.99	0.03-0.62	0.66-1.63	0.18-6.42
Measured temperature $\geq 38.3^{\circ}\text{C}$ <sup>16,22,23</sup>	1096	0.53	0.22-0.58	0.53-0.92	0.68-3.9	0.54-1.3
Nausea <sup>17,21</sup>	1941	0.52	0.26 (0.12-0.43)*	0.52-0.98	0.76-3.1	0.91 (0.86-0.97)*
Duration $<3$ d <sup>20,22</sup>	824	0.43	0.26-0.93	0.59 (0.54-0.64)*	0.72-3.5	0.15-2.2
Male sex <sup>21,22</sup>	1325	0.39	0.11-0.56	0.39-0.86	0.87 (0.72-1.05)*	1.1 (0.93-1.2)*
Palatine petechiae <sup>18,22</sup>	1202	NA	0.07 (0.02-0.14)*	0.95 (0.92-0.96)*	1.4 (0.48-3.1)*	0.98 (0.92-1.1)*
Strep exposure previous 2 wk <sup>18,19,22,23</sup>	2091	NA	0.19 (0.12-0.27)*	0.87-0.94	1.9 (1.3-2.8)*	0.92 (0.86-0.99)*
Rash <sup>17,21,22</sup>	2356	NA	0.04 (0.03-0.06)*	0.79-0.99	0.06-35	0.90-1.1

\*Where one of these operating characteristics was homogeneous ( $P > .05$  for the  $\chi^2$  test), the summary value and a 95% confidence interval (CI) are given. Where they are heterogeneous, only the range is given. Variables are given in the order of the area under the receiver operative characteristic curve, where one could be drawn. LR+ indicates positive likelihood ratio; LR-, negative likelihood ratio.

No individual element of history-taking or physical examination is accurate enough by itself to rule in or rule out strep throat.



# Testing for GAS

- **IDSA guidelines: Children under 3 years old should not be tested for GAS pharyngitis**
- Prevalence of GAS pharyngitis low for <3yo.
  - Estimated 10-14% with a positive test, but when ASO rise confirms, low as **0-6%**.
- iGAS cases without preceding pharyngitis
- Negligible risk for ARF\*





# Testing for GAS

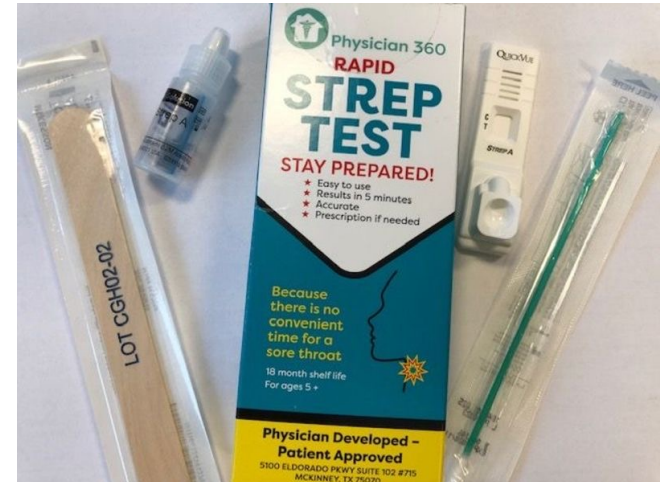
- **IDSA guidelines: Patients with viral symptoms should not be tested for GAS**
  - GAS carriage: 15-25% of children
  - Lack of viral symptoms have higher LR for GAS pharyngitis

**At-Home Tests for Influenza, Strep, Others, Raising Eyebrows of Some Experts**

Jun 17, 2019 | Madeleine Johnson

<https://www.360dx.com/immunoassays/home-tests-influenza-strep-others-raising-eyebrows-some-experts>

IDSA guidelines 2012



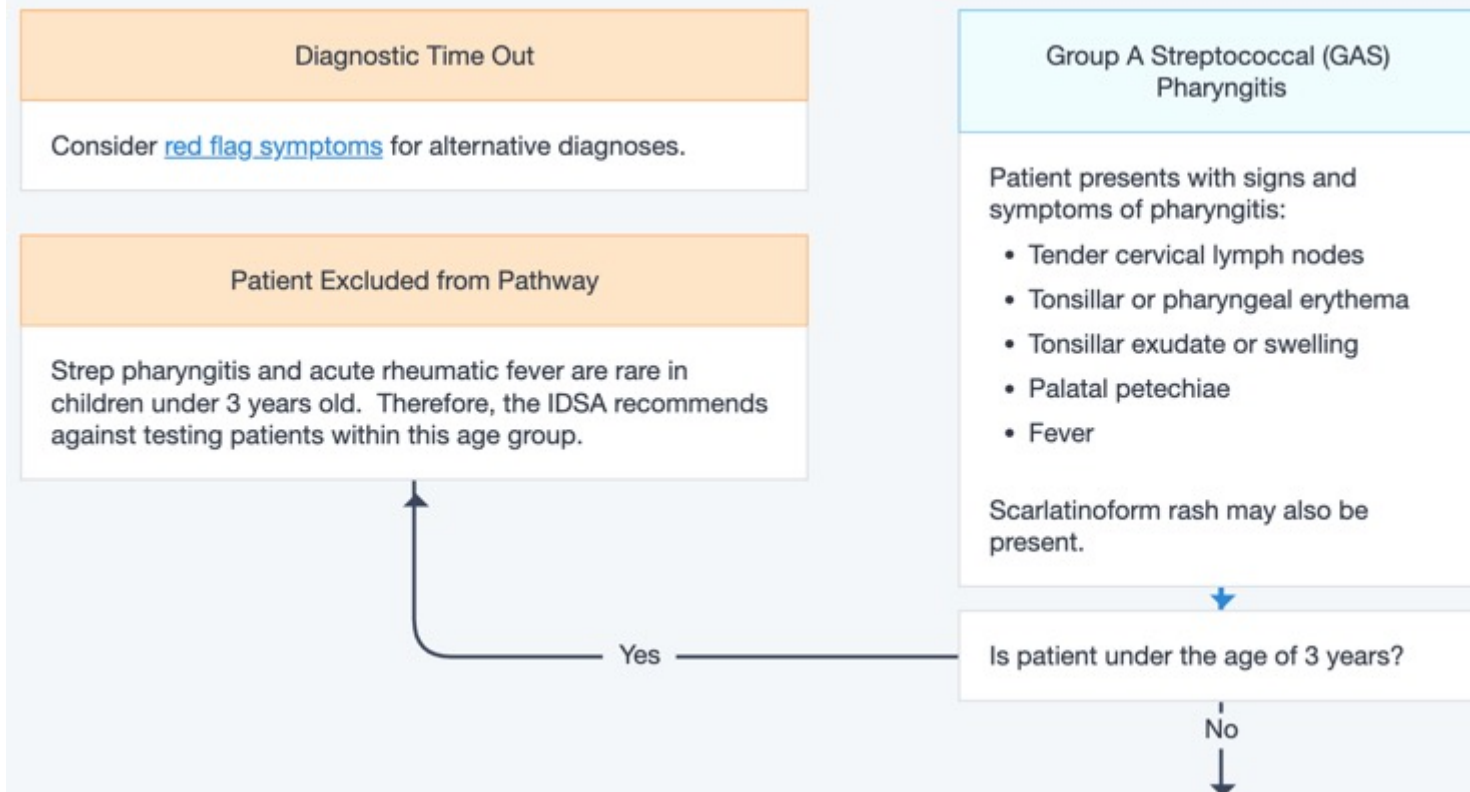


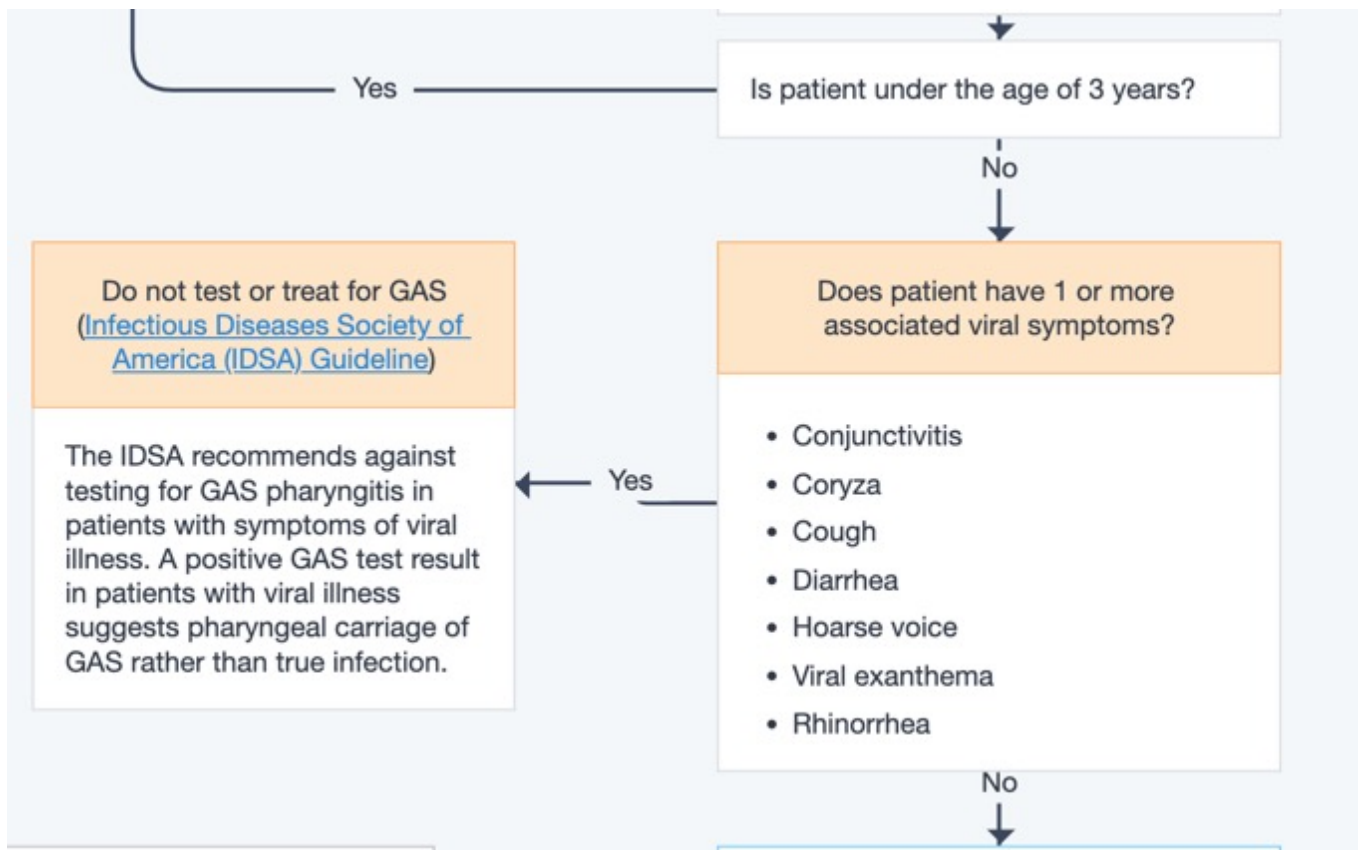
# Antibiotic Prescribing – all ages

Diagnosis	Percentage of diagnoses with antibiotic prescribed			
	UCC	Retail Clinic	ED	Medical Office
CAP	83%	91%	67%	67%
Pharyngitis	60%	57%	47%	51%
Sinusitis	82%	87%	68%	76%
AOM	83%	86%	72%	79%
All Dx	39%	36%	14%	7%

~15-37%







# Improving Guideline-Based Streptococcal Pharyngitis Testing: A Quality Improvement Initiative

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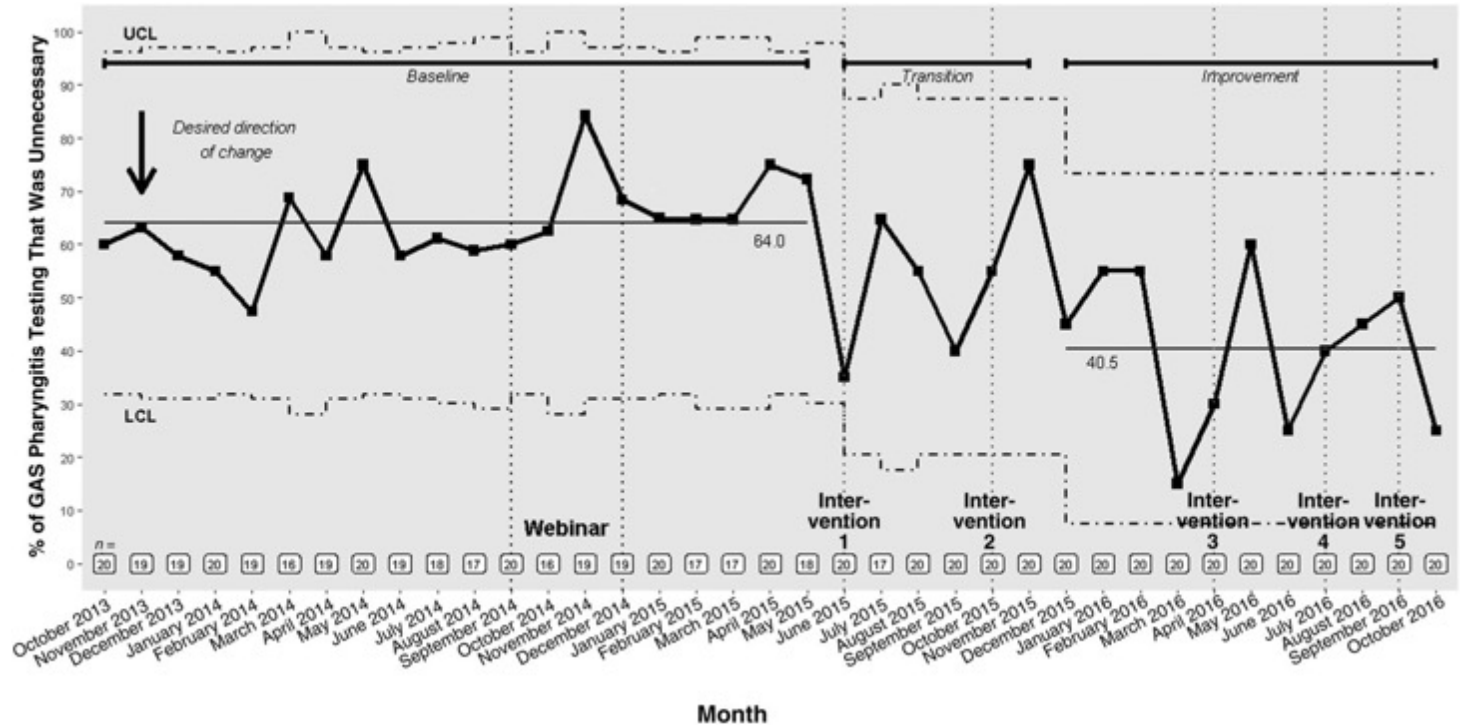
## Intervention:

- Education
- Removed standing orders for rapid GAS
  - Provider assessment required first
- Communication flier and strategies to parents

## Measured unnecessary GAS pharyngitis testing:

(1) age was <3 years and was without household contact with GAS pharyngitis, (2) presence of  $\geq 2$  viral symptoms, (3) had an absence of sore throat, **or** (4) had an absence of any expected GAS pharyngitis examination findings.

Pediatrics. 2018;142(1). doi:10.1542/peds.2017-2033



P-chart for the proportion of patients with unnecessary GAS pharyngitis testing over time. LCL, lower control limit; n, number of total charts included per month; UCL, upper control limit.

# Why do we treat strep throat?

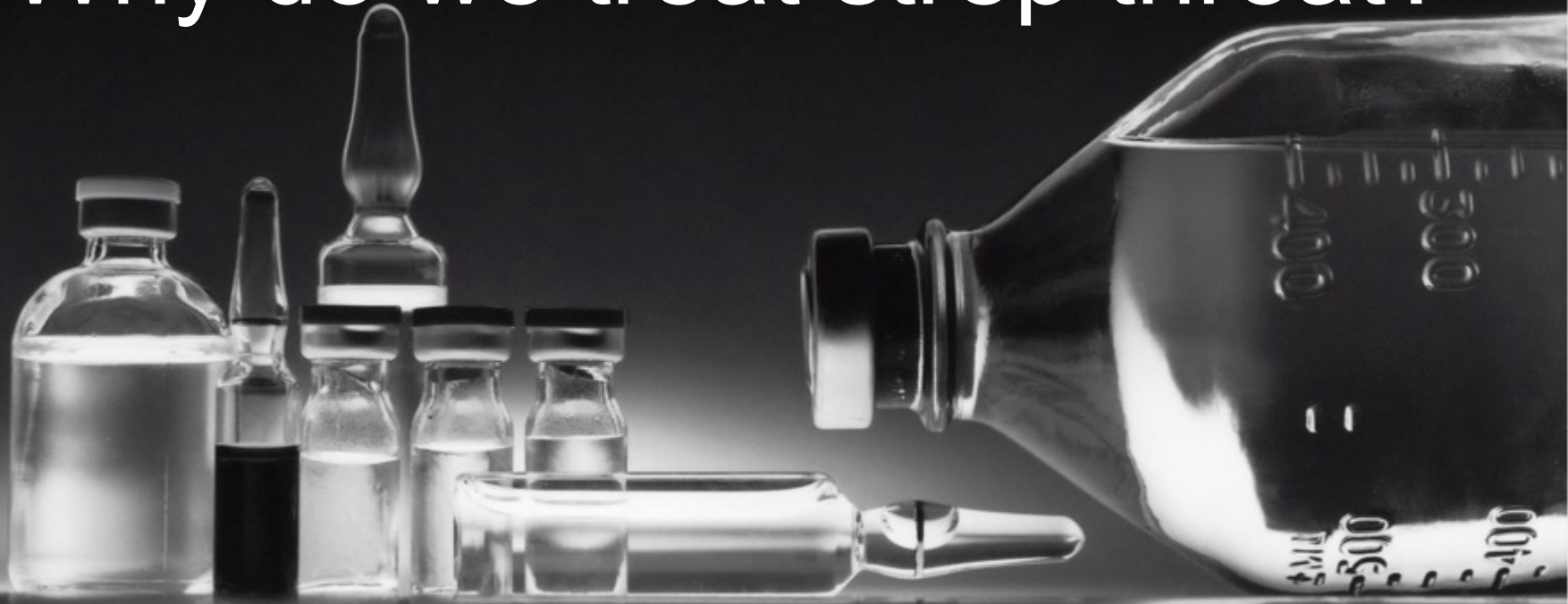


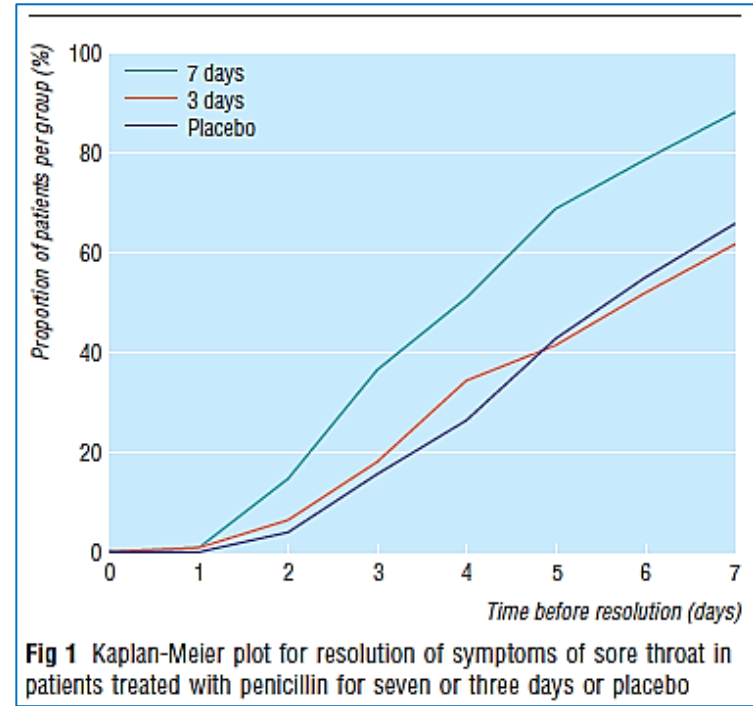
Photo by [National Cancer Institute](#) on [Unsplash](#)



# Improvement of symptoms



- Treated patients will feel better (fever, sore throat) about 16-24 hrs faster (3-4 vs. 4-5 days)
- Strep throat will self-resolve







# Prevent suppurative complications



Table 1| Characteristic of patients at index consultation. Values are numbers (percentages) unless stated otherwise

Characteristics	Not given antibiotics	Given antibiotics	Delayed antibiotics
Clinical assessment:			
Return <4 weeks with new or worsening symptoms	803/4974 (16.1)	864/5932 (14.6)	222/2382 (9.5)
Return <4 weeks with complications	75/4974 (1.5)	78/5932 (1.3)	21/2382 (0.9)
Individual complications:			
Quinsy Quinsy = abscess	11/4974 (0.2)	30/5932 (0.5)	6/2382 (0.3)
Sinusitis	23/4974 (0.5)	12/5932 (0.2)	3/2382 (0.1)
Otitis media	31/4974 (0.6)	27/5932 (0.5)	11/2382 (0.5)
Cellulitis or impetigo	10/4974 (0.2)	9/5932 (0.2)	1/2382 (0.0)

- Adult patients
- Clinical sx resolution & complications
- Complications RARE



# Prevent suppurative complications



Variables	No (%) with no complications	No (%) with complications	Univariate odds ratio (95% CI)	P value	Multivariate odds ratio* (95% CI)	P value
Earache†	642/13 163 (4.9)	25/177 (14.2)	3.22 (2.10 to 4.96)	<0.01	3.02 (1.91. to 4.76)	<0.01
Severely inflamed tonsils	1615/12 544 (12.9)	37/173 (21.4)	1.84 (1.28 to 2.66)	<0.01	1.92 (1.28 to 2.89)	<0.01

## Two predictors of suppurative complications:

- Ear ache (14% with complications, 5% without)
- Severely inflamed tonsils (13% w/ complications, 21% without)

## Reductions in abscess and AOM

NNTB 200 for OM, ~2000 for abscess

Does not appear to prevent glomerulonephritis



1950s military base: ARF occurred in 3-4% of those with pharyngitis

# Prevent ARF

<https://www.med-dept.com/articles/standard-terms-for-diagnoses-anatomical-locations-and-operations/>



1961 Chicago **0.33%** in untreated children with pharyngitis

High-risk countries: 50-500 per 100,000  
**0.05-0.5%, NNT 494**


Low-risk countries: 1-10 per 100,000  
**0.001-0.01%, NNT up to 1 million**

**US: 0.61 per 100,000**



<https://www.healthychildren.org/English/ages-stages/gradeschool/school/Pages/Back-to-School-Tips.aspx>

Siegel 1961



**CDC stopped  
tracking incidence  
of ARF in 1995:  
when it fell below  
1 per million**



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**University of Colorado**  
Anschutz Medical Campus

# 1953: 1<sup>st</sup> Guideline for treatment of GAS

“PCN is the drug of choice... Both the oral and the intramuscular administration have been utilized successfully in the treatment of streptococcal infections. IM injections have been proved to produce more rapid relief of symptoms. The data on the value of oral pcn as a preventative are less complete.”

Orals not studied for ARF

## 1955: Guideline update:

“Effective blood sterilization [with penicillin] should be maintained for a period of 10 days after the disappearance of the streptococci from the throat. Penicillin may be administered by either IM or oral route.”

Eradication not linked to ARF

TABLE 1. Duration of Antimicrobial Therapy for Common Infections

Year Published	Textbook	Meningitis	Pneumonia	Streptococcal Pharyngitis	Urinary Tract Infection	Acute Otitis Media
1942	Nelson	NDM	NDM	NDM	NDM	NDM
1945	Nelson	Clinical	NDM	NDM	Sterile urine	NDM
1950	Nelson	10 days	NDM	5 days	Sterile urine	NDM
1951	Harrison	NDM	Clinical	5-7 days	NDM	NDM
1954	Nelson	NDM	Clinical	10 days	Sterile urine	Clinical
1954	Harrison	2 weeks	Clinical	10 days	NDM	NDM
1958	Harrison	NDM	Clinical	10 days	10 days	NDM
1959	Nelson	10 days	Clinical	10 days	Sterile urine	Clinical
1962	Harrison	Clinical	Clinical	10 days	NDM	NDM
1964	Nelson	10 days	Clinical	10 days	1 month	Clinical
1966	Harrison	Clinical	Clinical	10 days	10 days	NDM
1969	Nelson	7 days	NDM	10 days	2 weeks	10 days
1970	Harrison	Clinical	Clinical	10 days	10 days	NDM
1974	Harrison	Clinical	Clinical	10 days	NDM	NDM
1975	Nelson	Clinical	7 days	10 days	2 weeks	10 days
1977	Harrison	Clinical	Clinical	10 days	10 days	NDM
1979	Nelson	10 days	10 days	10 days	2 weeks	2 weeks

NDM indicates no duration mentioned.

#### Comparison 4. Antibiotics versus control for the treatment of sore throat: incidence of complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Incidence of acute rheumatic fever within 2 months. Rheumatic fever defined by clinical diagnosis	17	12132	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.26, 0.50]
4.3.1 Incidence of acute rheumatic fever within 2 months: early (pre-1975) studies <b>Pre-1962</b>	10	7617	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.30 [0.20, 0.45]
4.3.2 Incidence of acute rheumatic fever within 2 months: late (post-1975) studies	5	2367	Peto Odds Ratio (Peto, Fixed, 95% CI)	Not estimable



A scanning electron micrograph (SEM) showing four bright yellow, spherical bacteria, likely Staphylococcus aureus, resting on a textured surface. The surface is composed of blue and orange-colored, irregular, and wavy structures, possibly representing host cells or a biofilm. The background is dark blue with some faint, out-of-focus particles.

What antibiotic do we use?

Photo by [National Cancer Institute](#) on [Unsplash](#)



### Positive Rapid Antigen Detection Tests (RADT) or PCR

- amoxicillin 50 mg/kg/dose (max: 1000 mg/dose) PO once daily x 10 days ([Inpatient](#)) ([Outpatient](#)) ([Treatment Duration Note](#)) **OR**
- penicillin G benzathine, 600,000 U (weight less than 27 kg); 1,200,000 U (weight greater than or equal to 27 kg) IM once

**OR**

- penicillin V PO ([Inpatient](#)) ([Outpatient](#))
  - Children Less than or Equal to 27 kg: 250 mg/dose PO every 8 to 12 hours for 10 days
  - Children Greater than 27 kg and Adolescents: 500 mg/dose PO every 8 to 12 hours for 10 days

If penicillin allergic:

- cephalexin 20 mg/kg/dose (max: 500 mg/dose) PO every 12 hours for 10 days ([Inpatient](#)) ([Outpatient](#))

Alternatives to penicillin or cephalosporin agents are available if needed. See [IDSA Guideline](#).

### Test for Group A Streptococcal

- Swab throat
- Conduct Rapid Antigen Detection Test (RADT) or PCR.

*Note: Testing choice of Positive Rapid Antigen Detection Tests (RADT) or PCR is based on lab availability at your location.*

Negative Rapid Antigen Detection Tests (RADT)

### Negative Rapid Antigen Detection Tests (RADT)

- Antibiotics are not indicated at this time
- Send Group A Streptococcal culture (unless sent previously)
- Treat pain (NSAIDs preferred):
  - ibuprofen 5-10 mg/kg every 6-8 hours (should not be used for patients younger than 6 months of age) ([Inpatient](#)) ([Outpatient](#))

**OR**

Positive Rapid Antigen Detection Tests (RADT) or PCR

Positive Culture

Negative PCR

Negative Culture



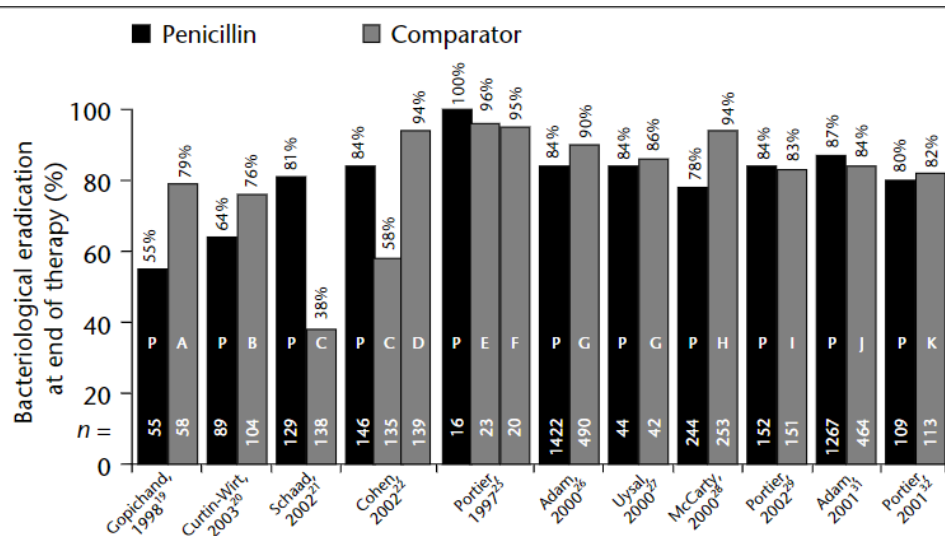
“There has never been a report of a clinical isolate of group A strep that is resistant to penicillin.”

-CDC





# Patients better but still test positive



**FIGURE 2:** Bacteriological eradication rates for penicillin versus comparator antibiotics at the end of therapy to treat tonsillopharyngitis caused by group A  $\beta$ -haemolytic streptococci. P, penicillin; A, amoxicillin 375 – 750 mg/day for 10 days; B, amoxicillin 35 mg/kg per day to 1 g/day for 10 days; C, azithromycin 10 mg/kg per day; D, azithromycin 20 mg/kg per day; E, cefpodoxime; F, amoxicillin/clavulanate; G, cefuroxime; H, clarithromycin; I, clarithromycin modified release; J, loracarbef; K, josamycin

- 11 studies  
– 1998-2003
- PCN eradication rates 55-100% - majority 80-90%



# Patients better but still test positive

## Clinical Studies

Duration of Group A *Streptococcus* PCR positivity following antibiotic treatment of pharyngitis

*J.H. Homme et al / Diagnostic Microbiology and Infectious Disease 90 (2018) 105–108*

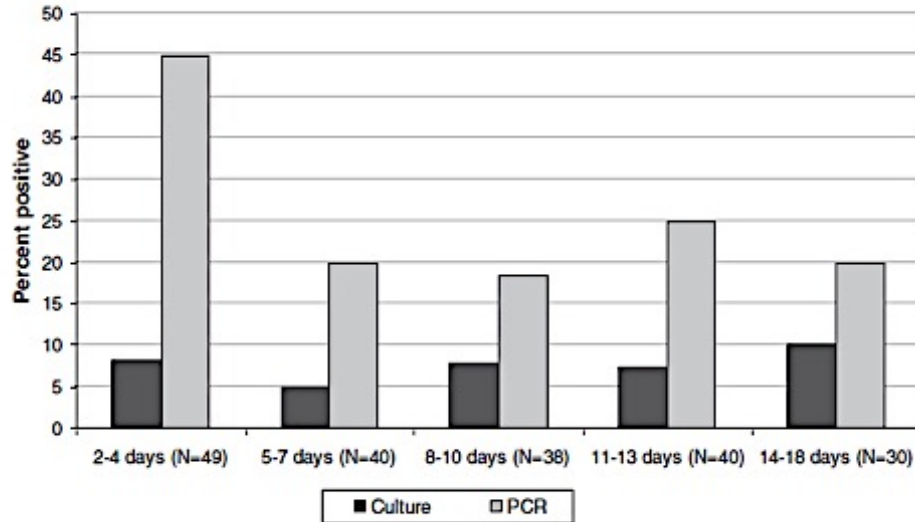


Fig. 1. Positive PCR and culture results by days from initial swab.

- Patients (n=50) all positive by PCR at day 0.
- All patients treated with AAP regimen (70% pcn)
- 5-10% still culture + at end of treatment



- IDSA guidelines: These children are considered 'bacteriologic failures'. Under most circumstances, these children are actually streptococcal carriers, and **further antimicrobial therapy is not warranted.**
- Persistent symptoms at 24-48h are most likely non-GAS pharyngitis. **Repeat testing is not recommended.**





# Should we try to decolonize?

## Carriers:

- unlikely to spread organism to their close contacts
- very low risk, if any, for developing suppurative or invasive complications or nonsuppurative complications
- difficult to eradicate GAS pharyngitis from the throats of carriers



# Once daily amoxicillin

- Amox 50mg/kg daily
- 4-6 days amoxicillin eradicates 90%
- Adult hypertensive study:  
**Compliance** improved from 59.0% on a three-time daily regimen to 83.6% on a once-daily regimen.

TABLE 1. Bacteriologic Response to Antibiotic Therapy

Feder et al, Pediatrics, 1999	Patients	No. of Positive Throat Cultures After Completion of Therapy*	
		4–6 Days <i>n</i> (%)	14–21 Days <i>n</i> (%)
Amoxicillin (once-daily)	79	9 (11)	4 (5)
Penicillin V (three times daily)	73	12 (16)	3 (4)



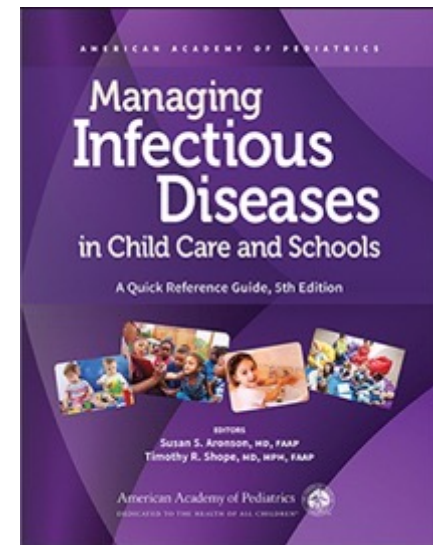
# Reduce contact transmission



## A Reappraisal of the Minimum Duration of Antibiotic Treatment Before Approval of Return to School for Children With Streptococcal Pharyngitis

Richard H. Schwartz, MD,\*† Danica Kim, BA,‡ Michael Martin, MD,\*† and Michael E. Pichichero, MD§¶

- Single dose of 50/kg amoxicillin
- n = 111 children
- GAS was not detectable in 91% (CI: 86–96%) at 11–23h after initial visit
- AAP ‘Purple Book’ – can return to class 12h after starting abx
- “Children infected w strep do not pose a risk to others once they have received their 1<sup>st</sup> 12h of abx treatment.





# Reduce contact transmission



- IDSA guidelines: against prophylaxis of asymptomatic contacts
- GABHS pharyngitis occurred in 54/1440 (3.8%) of siblings
- 30-day follow-up period
  - GABHS pharyngitis: 3.0% siblings in the prophylaxis group and 5.3% siblings in the control group ( $P=0.040$ ).
    - Cephalosporin group was 1.8% vs 5.3% in control group ( $P=0.003$ )
    - Penicillin group was 4.3% vs control group ( $P=0.542$ ).
- Guideline recommendations account risk vs harm



# Minimize adverse effects of inappropriate abx therapy

- Anaphylaxis to penicillin: 1-5 per 10,000 courses
- Penicillin allergy reported in 1 in 10 patients → labeled allergy (#1 reason: rash)



# Minimize adverse effects of inappropriate abx therapy

- Resistance in outpatient conditions increasing
  - Receipt of 1 course of any antibiotic within 6 months is risk factor for drug-resistant UTI (OR 1.6)
- Increased risk of inflammatory bowel disease, juvenile idiopathic arthritis, and obesity
  - Cumulative effect (every dose counts!)
- ED visits for adverse drug events
  - 0-5 y/o: 56% of ED visits for adverse drug events (e.g., diarrhea, rash, anaphylaxis)





# Minimize adverse effects of inappropriate abx therapy



Patient-Centered Outcomes in the Prospective Cohort

Outcome	No./Total (%) <sup>a</sup>		Stratified Analysis <sup>b</sup>	
	Broad-Spectrum Antibiotics	Narrow-Spectrum Antibiotics	Risk Difference (95% CI), % <sup>d</sup>	P Value
Missed school or day care	305/702 (43.4)	503/1199 (42.0)	2.5 (-3.9 to 9.0)	.45
Required additional childcare	220/701 (31.4)	390/1190 (32.8)	-0.2 (-5.7 to 5.2)	.94
Experienced adverse events	258/725 (35.6)	341/1360 (25.1)	11.6 (6.0 to 17.2)	<.001
Symptoms present on day 3 <sup>f</sup>	267/647 (41.3)	427/1128 (37.9)	2.3 (-4.5 to 9.1)	.50
Sleep disturbance	378/860 (44.0)	582/1570 (37.1)	4.6 (-0.5 to 9.6)	.08
Pediatric Quality of Life Inventory score <sup>g</sup>	(n = 860)	(n = 1570)	-1.6 (-2.8 to -0.5) <sup>i</sup>	.006
	90.2 (10.5) <sup>h</sup>	91.5 (9.4) <sup>h</sup>		

- Prospective 10,000 children (6mos-12y)
- Dx with AOM, GAS, or Acute Sinusitis

25% narrow spectrum w adverse events

- Diarrhea 70%
- Rash 40.1%
- Upset stomach +/- vomiting 20%
- > 1 adverse event 28%

**1 in 4 children**  
on penicillin or amoxicillin will  
have an adverse drug event.

**~1 million children**  
receive antibiotics to prevent  
1 case of RHD in the US





# Durations for desired outcomes



Prevent acute  
rheumatic  
fever

Do we even  
need to treat at  
all??



Prevent  
suppurative  
complications

? NNT~200  
Treat the  
complication.



Improve  
clinical  
symptoms

~1-3days  
(for 16-24h  
benefit)



Reduce  
transmission  
to close  
contacts

12 hours



Minimize  
adverse  
effects of  
inappropriate  
antimicrobial  
therapy

As few as  
possible

Low-risk countries:  
NNT ~1 million

Clinical endpoints for  
duration decisions



	<b>GAS Pharyngitis Durations</b>
<b>United States</b>	10 days
<b>United Kingdom (NICE)</b>	5 days for symptomatic cure 10 days for microbiologic cure
<b>The Netherlands</b>	Forego antibiotics  If treating, 5-7 days to shorten symptom duration
<b>Australia</b>	High-risk groups: 10 days Low-risk groups: forego antibiotics
<b>WHO</b>	High-risk groups: 10 days Low-risk groups: forego antibiotics. If treating low-risk: 5 days



# What about compliance?

		Duration of Treatment (Days)		Compliance	
				<i>n</i>	%
Tonsillopharyngitis	231	<7		47/63	74.6
Otitis media	170	7		116/147	78.9
Lower respiratory tract infection	114	>7-<10		47/74	63.5
Sinusitis	23	≥10		196/300	65.3

- Chicago: RCT (2009-2015) for skin infection: full duration adherence (10d) was 38%
- Isreal: in GAS pharyngitis, most parents stop abx 1-2d after fever stopped
- Atlanta: 16% of parents store abx at home, most residual from previous prescription





- Amox shortage → 5d
- 5 days studied in cephalosporins and accepted
- 10d is historical from 1940's when duration was studied
- ARF as outcome can only be studied in high risk populations. US to low.
- Other low-risk nations: 0 or 5d

#### Treatment Duration Consideration



Consider a shorter duration of therapy (e.g. 1-5 days) for Group A Streptococcal pharyngitis for the following reasons:

- Children are no longer contagious after 1 dose of amoxicillin (50mg/kg/dose). (Schwartz 2015; Shope 2019)
- Symptoms will improve/resolve in 1-3 days after antibiotic treatment for Group A Streptococcal pharyngitis.
- Short courses of amoxicillin, including single dose, demonstrate similar decrease in microbiologic burden as longer courses of penicillin. (Feder 1999; Homme, 2018)
- There are no statistically robust studies and no studies in children demonstrating 10 days of oral antibiotics are needed to prevent acute rheumatic fever.
- Longer durations of therapy cause increased adverse drug events and higher rates of bacterial antibiotic resistance.





# Take Away Points

- Strep pharyngitis does not progress to iGAS
- GAS pathway at CHCO
- Children <3yo or with viral symptoms: no test
- Carriers often still carriers after tx → don't retest
- ARF incredibly rare
- Consider 5d durations



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## Keeping Colorado Healthy, One Antibiotic Choice at a Time.

EXPLORE FIRSTLINE

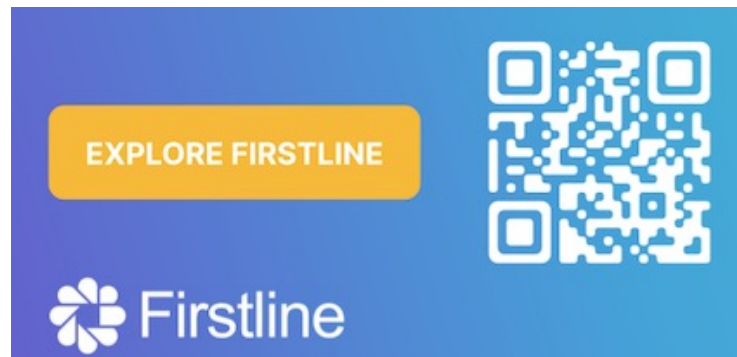


Firstline





# Thank you!



[Nicole.Poole@ChildrensColorado.org](mailto:Nicole.Poole@ChildrensColorado.org)