Croup Pathway v4.0: Table of Contents



Inclusion Criteria

- · Previously healthy children
- Age 6 months to 6 years

Exclusion Criteria

- Toxic appearance
- · Symptoms suggestive of an alternative diagnosis
- Known upper airway abnormality
- Hypotonia or neuromuscular disorder

Croup Care

ED Management

Inpatient Management

Appendix

Summary of Version Changes

Approval & Citation

Evidence Ratings





Croup Pathway v4.0: ED Management

Stop and **Review** diagnosis Signs of impending respiratory failure **Poor respiratory effort** Stridor may be present or decreased **Listless or decreased LOC** Cyanosis / Hypoxemia acceptable) Tachypnea Consider **BACTERIAL TRACHEITIS** No in children who appear toxic or have poor response to racepinephrine Give **Dexamethasone** (if not previously given) Evaluate Dosage of 0.6mg/kg Dexamethasone criteria for Steroids are beneficial for all patients Racemic epinephrine with croup Discharge criteria not met **Observation with Respiratory Assessment Q1 hour** If worsening or not meeting discharge Meets criteria consider racepinephrine discharge criteria Meets discharge criteria **Discharge Criteria** Minimal stridor at rest (stridor with activity to be expected) Minimal retractions Meets Able to talk or feed without difficulty ←Discharge 2 hours since racepinephrine criteria **Discharge Instructions** Return for increased work of breathing

Recommendations 1. Consider OTO consultation/referral for

direct laryngoscopy in patients with 2 or

more episodes of croup and that have a

months or who have prolonged severe

2. Consider evaluation for GERD and

initiation of anti-reflux medications in

3. Consider evaluation and treatment for

allergies

Last Updated: September 2020

Next Expected Review: September 2025

history of intubation and age less than 36

disease requiring inpatient management.

patients with prolonged or recurrent croup

Inclusion Criteria

- · Previously healthy children
- Age 6 months to 6 years

Exclusion Criteria

- Toxic appearance
- Symptoms suggestive of an alternative
- Known upper airway abnormality
- Hypotonia or neuromuscular disorder

Pathophysiology

Not Recommended No evidence supporting the use

- Viral PCR
- Radiographs
- Repeat Dexamethasone
- Cool Mist

Severity Assessment (moderate / severe distress)

Stridor at rest AND one or more of the following:

- Moderate intercostal retractions (suprasternal retractions are
- Agitation / restlessness / tired appearing Y
- Difficulty with talking or feeding

Give Racemic Epinephrine

• Racepinephrine 2.25% inhalation solution (0.5 mL nebulized) diluted in 3 mL NS. Goal is within 30min of arrival

AND

Give **Dexamethasone** (if not previously given)

Not

Improved

Dosage of 0.6mg/kg Dexamethasone

Assess immediate clinical response

Severity Assessment (moderate / severe distress)

Stridor at rest AND one or more of the following:

- Moderate intercostal retractions (suprasternal retractions are acceptable)
- Tachypnea
- Agitation / restlessness / tired appearing
- Difficulty with talking or feeding

Improved

Observation for 2 hr with minimum Q1 hour <u>assessments</u>

- Racepinephrine effect lasts only 2 hours
- If patient worsens, consider repeat racepinephrine and admission

Does not meet Discharge Criteria

Admit Criteria

- · Patients with continued stridor at rest AND any symptoms listed in the severity assessment above
- Patients receiving 3 or more doses of racepinephrine
- Patients not otherwise meeting discharge criteria

that are not improving with 3 doses of racepinephrine, consider further workup, OTO consultation, and/or evaluation for ICU

For children

- Give 2nd dose of nebulized epinephrine immediately if croup symptoms are not improved
- · Consider Heliox with severe croup in patients at risk of losing their airway during transport and admission to **ICU**
- Consider alternative diagnosis or ICU admission

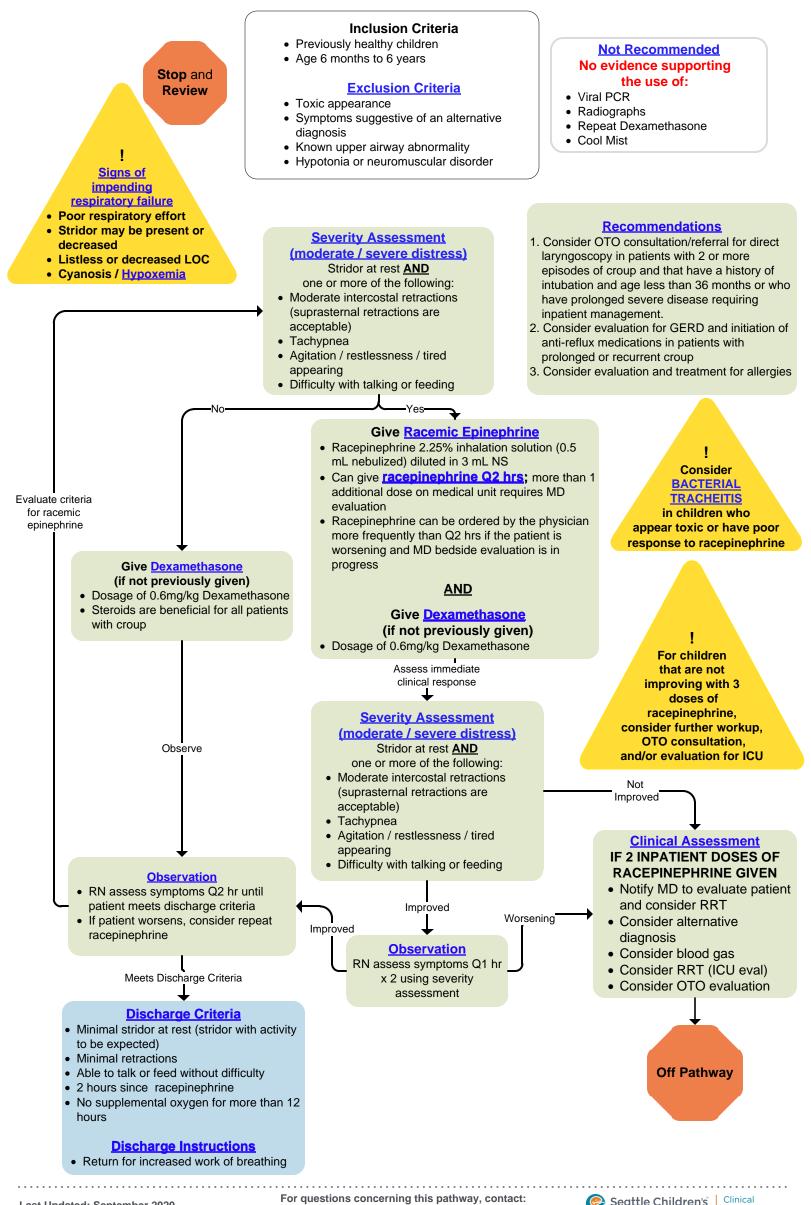


Urgent Care Transfer Criteria

- Poor initial response to 1st Racepinephrine
- If 2nd Racepinephrine given
- ALS recommended for all patients. Can repeat Racepinephrine while awaiting transportation if necessary.

To Inpatient Management

Croup Pathway v4.0: Inpatient Management



Last Updated: September 2020

Next Expected Review: September 2025

Exclusion Criteria

- Toxic Appearance
- Symptoms suggestive of an alternative diagnosis:
 - o Poor response to treatment with racemic epinephrine
 - o Expiratory wheeze
 - o Drooling or difficulty swallowing
 - o Prolonged or recurrent stridor
- Known upper airway abnormality
 - o Laryngomalacia
 - o Tracheomalacia
 - o History of vascular ring/sling or tracheoesophageal fistula
- Hypotonia or neuromuscular disorder resulting in hypotonia
 - o Trisomy 21

Therapies NOT Indicated in Croup

Not Recommended

No evidence supporting the use of:

- Viral PCR
- Radiographs
- Repeat Dexamethasone
- Cool Mist

Background Croup

- Also known as laryngotracheobronchitis
- Viral illness
- Most common in late fall to early winter
- Results in inflammation and swelling of the upper airway
- Most commonly caused by Parainfluenza virus
- Other causes include:
 - o Respiratory syncytial virus
 - o Influenza A and B
 - o Mycoplasma Pneumoniae
 - Other respiratory viruses

Symptoms

- Sudden onset of barky cough
- Inspiratory stridor
- Hoarse voice
- Respiratory distress
- Can be accompanied by fever
- May be abrupt in onset or be preceded by mild URI symptoms

Natural Course

- Symptoms are usually worse at night
- Usually resolve within 48 hours
- Often followed by upper respiratory infection type symptoms

Warning Signs: Alternative Diagnoses

IMPORTANT Guidance

 Bacterial tracheitis can mimic croup initially, but if not identified early can lead to high morbidity and mortality

Review of serious safety events involving the initiation of the croup pathway demonstrate that a patient that is not responding to racepinephrine needs further physician evaluation to consider alternative diagnoses and escalation of care

Consider
BACTERIAL
TRACHEITIS
in children who
appear toxic or have poor
response to racepinephrine

Bacterial Tracheitis

- Rapidly progressive
- Requires prompt assessment of airway by otolaryngology and possible intubation in a controlled setting
- Symptoms suggestive of bacterial tracheitis:
 - URI symptoms have been present >24 hours
 - Fever may/may not be present
 - Symptoms do not respond or show incomplete response to racepinephrine
 - CRP and WBC are not predictive for or against bacterial tracheitis
 - Patients may have an oxygen requirement (unusual in croup)

Severity Assessment

Upon presentation and after each intervention the patient should be assessed for moderate to severe respiratory distress.

In croup, moderate to severe respiratory distress is defined as:

- Stridor at rest
- AND one or more of the following:
 - Moderate intercostal retractions (suprasternal retractions are acceptable)
 - o Tachypnea
 - Agitation / Restlessness / Tired appearing
 - Difficulty talking or feeding

Severity Assessment (moderate / severe distress)

Stridor at rest **AND** one or more of the following:

- Moderate intercostal retractions (suprasternal retractions are acceptable)
- Tachypnea
- Agitation / restlessness / tired appearing
- Difficulty with talking or feeding

Focuses on specific symptoms that indicate a need for racemic epinephrine (moderate to severe symptoms):

- Provides a common language to discuss the severity of symptoms among patients
- Based on the Westley Croup Score (Westley 1978)

Recurrent Croup

- Defined as 2 or more episodes of croup
 - Can be infectious or spasmodic
- Occurs in about 6.4% of children
 - Historically in our institution (between August 2011 and January 2013), we found 5.3% (36/683) patients presented with 2 or more croup encounters
- Two studies demonstrated an association with atopy
 - o 36-44% of patients with recurrent croup have a history of atopy.
- 4 studies demonstrated evidence of GERD
 - Identified via laryngoscopy findings
 - Occurrence ranged from 28-87.2% of patients studied.
- Chart review of Seattle Children's patients with recurrent croup demonstrated an association with:
 - o prior intubation (29% in cases vs. 0%in controls)
 - history of asthma (21% in cases vs. 1% in controls)
 - o prematurity (14% in cases versus 0.09% in controls).

2020 Findings

History of Endotracheal Intubation in children with recurrent croup

History of intubation was compared to never intubated in 3 cohort studies (n = 419 participants) of children with recurrent croup to evaluate the risk for abnormal bronchoscopy findings. We are moderately confident that the variation in risk associated with history of intubation (probability of future abnormal bronchoscopy findings in those with the prognostic factor) is likely to be OR 5.2 (95% CI: 2.6 to 10.1), but there is a possibility that it is substantially different (event rates 4.9% if never intubated versus 22.1% if history intubation). Assuming 4.9% of patients with no history of intubation experience abnormal bronchoscopy findings, a history of intubation increases the absolute risk of abnormal bronchoscopy findings by 14.8% (95% CI: 9.3% to 18.6%) given an overall population prevalence of history of intubation of 32.4% and abnormal bronchoscopy findings of 10.5%. This outcome is downgraded due to bias; model adjusting for multiple prognostic factors was not used [LOE +3 moderate certainty (Hiebert 2016)].

History of Prematurity in children with recurrent croup

Children with recurrent croup and a history of prematurity in 2 cohort studies (N=316) have a higher risk of abnormal bronchoscopy findings compared the those with normal gestation. OR 2.90 (1.39 to 6.06) [LOE +3 moderate certainty; downgraded for bias (Hiebert 2016)].

History of Inpatient Consultation in children with recurrent croup

Children with recurrent croup and a history of inpatient consultation in 3 cohort studies (N=416) had significant increased risk of abnormal bronchoscopy findings vs children with no such history. OR 4.01 (1.44 to 11.20). [LOE +3 moderate certainty; downgraded for bias (Hiebert 2016)].

Recurrent Croup continued

2015 Findings

- Moderate to severe operative findings (i.e., findings that require intervention) were found in 8.7% of patients with recurrent croup (65.0% had normal findings and 26.2% had mildly abnormal findings) [LOE +1 Very low quality (Delaney, 2015)]
- Two studies attempted to find risk factors significantly associated with moderate to severe operative findings. Both found the following risk factors:
 - Inpatient consultation
 - History of intubation
- Delany (2015) also found increased risk associated with Age < 36 months and seasonal allergies. LOE +1 Very low quality
- Jabbour (2011) found prematurity to also be an associated risk factor. LOE +1 Very low quality
- Both studies suggest benefit to performing laryngoscopy in patients with previous intubation and age < 1 year (Jabbour) or < 3 years (Delany) and for patients who require inpatient consultation.

Recurrent Croup Recommendations

Recommendations

- Consider OTO consultation/referral for direct laryngoscopy in patients with 2 or more episodes of croup and that have a history of intubation and age less than 36 months or who have prolonged severe disease requiring inpatient management.
- Consider evaluation for GERD and initiation of anti-reflux medications in patients with prolonged or recurrent croup
- 3. Consider evaluation and treatment for allergies

- Otolaryngology evaluation can occur as inpatient or outpatient, depending on the severity of presentation.
- Evaluation for GERD and atopy can be conducted by the medical team or PCP.

Dexamethasone

Dexamethasone is recommended for *ALL patients* presenting with croup symptoms.

Give <u>Dexamethasone</u> (if not previously given)

- Dosage of 0.6mg/kg Dexamethasone
- · Steroids are beneficial for all patients with croup

Findings

- Author (Gates 2018) recommendations: Conclusions for 2019 Cochrane Systematic Review for Croup were changed from the 2011 version to report glucocorticoids significantly reduces croup signs and symptoms within 2 hours in addition to the previous 6-hour metric.
- Glucocorticoids are associated with an improved croup score at 6 hours (-1.2 points) and at 12 hours (-1.9 points); NNT for improvement = 5
- Fewer return visits in patients treated with glucocorticoids compared to placebo
- Length of hospital/ED stay was significantly decreased (mean decrease of 12 hours)
- Use of epinephrine is decreased

[LOE: +3, (Russell, 2011)]

Dexamethasone Dosage

A dosage of 0.6 mg/kg of dexamethasone should be given

- Maximum dose of 16mg
- Round dose to nearest 2mg dosage

Rationale

Dexamethasone 0.6 mg/kg IM reduces 2 hour Croup Score slightly more compared to Dexamethasone 0.15 mg/kg IM [mean difference MD -0.15 croup score (95% CI: -0.29 to -0.01)]. Very low N = 41; [LOE: +2 Low certainty (Gates 2018)].

"In the absence of further evidence, a **single** oral dose of dexamethasone, probably 0.6mg/kg, should be preferred because of its safety, efficacy and cost effectiveness."

- Most of the studies that compared dexamethasone to placebo used the dosage of 0.6mg/kg (12 of 31 trials; N=2032)
- There are small studies showing similar therapeutic effect at lower doses, more studies need to be done before changing the dosing recommendation.

[LOE: +3, (Russell, 2011), (Dobrovoljac, 2012)]



Dexamethasone continued

Comparison between steroids

- Combination of dexamethasone + budesonide is no better than dexamethasone or budesonide alone
- No difference between PO and IM dexamethasone
- Dexamethasone and prednisolone are equally effective at 6 and 12 hours, but readmission is more likely with prednisolone

[LOE: +3, (Russell, 2011)]



Racemic Epinephrine (racepinephrine)

Racemic Epinephrine (racepinephrine)

Racemic epinephrine works by causing mucosal vasoconstriction and reduction of subglottic edema.

- Nebulized epinephrine is associated with clinically and statistically significant transient reduction of symptoms of croup at 30 minutes post-treatment. (3 studies, 94 children)
- Evidence does not favor racemic epinephrine or L-epinephrine, or Intermittent Positive Pressure Breaths (IPPB) over simple nebulization.
- Treatment effect disappears after two hours.
- There is no evidence, on average, to suggest that there was an increase or worsening of croup score, as compared to the pre-treatment or baseline in the group treated with epinephrine.

[LOE: +3, (Bjornson, 2013)]

Who should receive it?

- Children with severe respiratory distress (indicated by marked sternal wall indwelling and agitation) [LOE: E (Expert Opinion), (Toward Optimized Practice, 2008)]
- Children with severe or life threatening croup. [LOE: Guideline, (Mazza, 2008)]
- Compared with placebo or no treatment nebulized adrenaline is more effective in the short-term at reducing symptom severity at 10-30 minutes in children with moderate to severe croup. [LOE: , (Johnson, 2004)].

<u>Severity Assessment</u> (moderate / severe distress)

Stridor at rest AND

one or more of the following:

- Moderate intercostal retractions (suprasternal retractions are acceptable)
- Tachypnea
- · Agitation / restlessness / tired appearing
- · Difficulty with talking or feeding

= Moderate/Severe



Racemic Epinephrine: Observation in the ED

Observation for 2 hr with minimum Q1 hour assessments

- Racepinephrine effect lasts only 2 hours
- If patient worsens, consider repeat racepinephrine and admission
- Treatment effect disappears after two hours.
- There is no evidence, on average, to suggest that there was an increase or worsening of croup score, as compared to the pretreatment or baseline in the group treated with epinephrine.

[LOE: +3, (Bjornson, 2013)]

Racemic Epinephrine: Inpatient Management continued

Racemic epinephrine can be given every 2 hours to patients who meet severity criteria.

We strongly recommend that patients be reevaluated by MD if requiring more than **ONE** additional dose of racemic epinephrine after admission.

Racemic epinephrine can be given more frequently than Q2 hours, but should be done cautiously in conjunction with ongoing MD evaluation.

Give Racemic Epinephrine

- Racepinephrine 2.25% inhalation solution (0.5 mL nebulized) diluted in 3 mL NS
- Can give racepinephrine Q2 hrs; more than 1 additional dose on medical unit requires MD evaluation
- Racepinephrine can be ordered by the physician more frequently than Q2 hrs if the patient is worsening and MD bedside evaluation is in progress

AND

Give Dexamethasone (if not previously given)

Dosage of 0.6mg/kg Dexamethasone

Racemic Epinephrine: Cautions!

Most patients with croup demonstrate rapid and significant improvement of symptoms with administration of racemic epinephrine.

Consider further workup and removal from the croup clinical pathway if your patient does not show improvement with administration to racemic epinephrine.



Racemic Epinephrine: Clinical Assessment

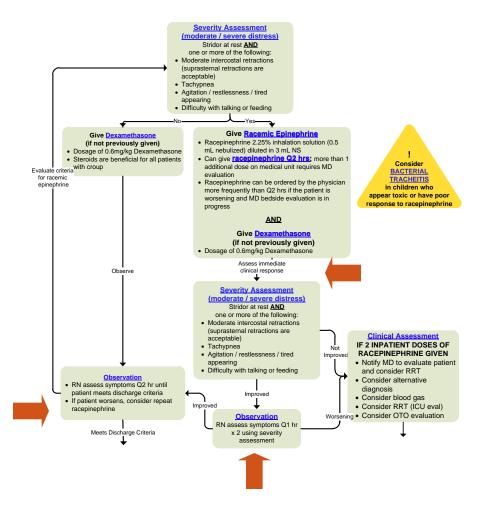
We have added an important safety step to help identify patients who may be at high risk for deterioration or alternative diagnoses.

Clinical Assessment

IF 2 INPATIENT DOSES OF RACEPINEPHRINE GIVEN

- Notify MD to evaluate patient and consider RRT
- Consider alternative diagnosis
- Consider blood gas
- Consider RRT (ICU eval)
- Consider OTO evaluation

Discharge Criteria: Inpatient



RN will assess severity symptoms upon transfer to the medical unit.

If racemic epinephrine given, observe patients hourly for 2 hours.

Assess discharge readiness every 2 hours after arrival to floor.

Patient can be discharged as soon as discharge criteria are met.

Discharge Criteria

- Minimal stridor at rest (stridor with activity to be expected)
- Minimal retractions
- Able to talk or feed without difficulty
- 2 hours since racepinephrine
- No supplemental oxygen for more than 12 hours

Discharge Instructions

Return for increased work of breathing

Signs of Failure

One in 4,500 children (1 in 170 hospitalized children) with croup are intubated. [LOE: E (Expert Opinion), (Toward Optimized Practice, 2008)]

Hypoxemia is uncommon in otherwise healthy children with croup and should be viewed as a warning sign of possible respiratory failure

!
Signs of impending respiratory failure

- Poor respiratory effort
- Stridor may be present or decreased
- Listless or decreased LOC
- Cyanosis / Hypoxemia

Discharge Criteria: Emergency Department

Discharge Criteria

- Minimal stridor at rest (stridor with activity to be expected)
- Minimal retractions
- Able to talk or feed without difficulty
- 2 hours since racepinephrine

Discharge Instructions

• Return for increased work of breathing

Study of children (n=527) admitted to hospital with stridor and/or sternal retractions at rest showed that only 1% of those who had resting stridor but no sternal retractions (N=305) had worsening respiratory distress after admission. (Wagner 1986)

A child with croup who received adrenaline and steroids may be discharged after 3 hours observation if they are free of stridor and intercostal retractions at rest and are clinically well. [LOE: Guideline, (Mazza, 2008)]

Criteria for ED discharge:

- Presence of mild symptoms either on initial evaluation or after a period of observation
- Children should not be discharged earlier than 2 hours after the administration of adrenaline
- Parents should be able to return for care if symptoms worsen [LOE: E (Expert Opinion), (Toward Optimized Practice, 2008)]

Transfer Criteria from Urgent Care to ED

We recommend transfer to the ED of all croup patients who are not initially responding to epinephrine due to risk of decompensation and all patients who meet admission criteria.

Due to possible respiratory compromise in transit, ALS is recommended.

Urgent Care Transfer Criteria

- Poor initial response to 1st Racepinephrine
- If 2nd Racepinephrine given
- ALS recommended for all patients.
 Can repeat Racepinephrine while awaiting transportation if necessary.

Admission Criteria

There is evidence that healthy children with mild croup do not need admission to the hospital

There is no evidence that stratifies the risks/ benefits of whom to admit in the moderate category

There is consensus that patients with severe croup should be admitted

Local data shows that patient receiving 3 or more doses of recepinephrine hae a more severe course / presentation and may benefit from admission.

Observation with Respiratory Assessment Q1 hour

If worsening or not meeting discharge criteria consider racepinephrine

Discharge criteria not met

Admit Criteria

- Patients with continued stridor at rest AND any symptoms listed in the severity assessment above
- Patients receiving 3 or more doses of racepinephrine
- · Patients not otherwise meeting discharge criteria

To Inpatient Management

Discharge Instructions

For patients being discharged from the emergency room, discharge instructions will be provided.

Call your Primary Health-Care Provider or return to the Emergency Department if your child:

- Breathing becomes more difficult or does not improve with moist air treatments and calming techniques as listed above
- Has stridor at rest when calm and is working hard to breathe
- Has trouble swallowing or is drooling a lot
- Is not able to take liquids
- Shows signs of dehydration:
 - dry mouth
 - no tears when crying
 - o urinates less than 3 times in 24 hours
- Is too fussy or cannot be calmed
- Is too sleepy
- Seems sicker

Discharge Instructions

Return for increased work of breathing

Call 9-1-1 if your child:

- Is having a hard time breathing
- Lips or face look blue

Summary of Version Changes

- Version 1.0 (12/19/2011): Go live
- **Version 1.1 (05/31/2012)**: Updated Viral FA to Viral PCR. Correction to Alternative Diagnosis slide: upset changed to onset
- **Version 2.0 (08/19/2015)**: Scheduled review update (see executive summary for significant changes)
- Version 3.0 (02/04/2019): Removed "Patients receiving 2 doses of racepinephrine" from admission criteria
- **Version 4.0 (09/22/20):** Periodic Review resulted in added treatment if patient does not improve in ED Phase and an updated Bibliography.

Approval & Citation

Approved by the CSW Croup Pathway team for September 22, 2020 go-live

CSW Croup Pathway Team:

Inpatient Medicine, Co-Owner Emergency Department, Co-Owner

Medical Unit, CNS Team Member ED/UC, CNS Team Member

Julianne Biship, MD Brianna Enriquez, MD

Missy Lein, MSN, RN, PCNS-BC Sara Fenstermacher, RN, MSN, CPN

Clinical Effectiveness Team:

Consultant **Project Manager Data Analyst** Librarian

Program Coordinator

Jean Popalisky, DNP

Dawn Hoffer, PMP, SCPM

James Johnson Sue Groshong Kristyn Simmons

Clinical Effectiveness Leadership:

Medical Director Operations Director Darren Migita, MD Jaleh Shafii, RN, MS

Retrieval Website:

Retrieval Website: https://www.seattlechildrens.org/pdf/Croup-pathway.pdf

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Evidence Ratings

This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children's. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94, Hultcrantz M et al. J Clin Epidemiol. 2017;87:4-13.):

Quality ratings are downgraded if studies:

- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings are *upgraded* if it is felt that:

- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

Certainty of Evidence

QQQQ High: The authors have a lot of confidence that the true effect is similar to the estimated effect

♥♥♥○ Moderate: The authors believe that the true effect is probably close to the estimated effect

QQ○○ Low: The true effect might be markedly different from the estimated effect

OOO Very low: The true effect is probably markedly different from the estimated effect

Guideline: Recommendation is from a published guideline that used methodology deemed acceptable by the team Expert Opinion: Based on available evidence that does not meet GRADE criteria (for example, case-control studies)

Bibliography

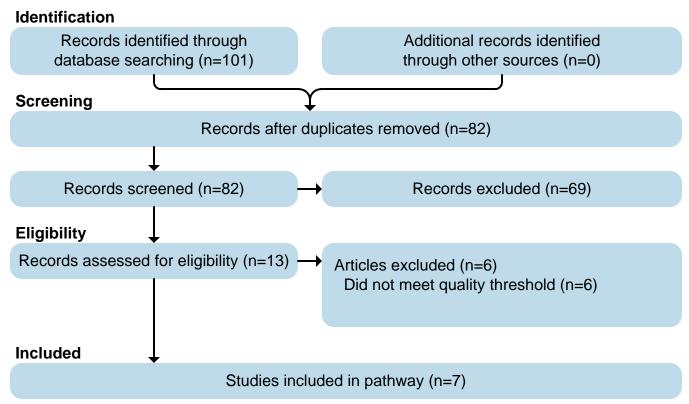
Literature Search Methods

For this update, we revised the search strategies in line with current Library practices. A literature search was conducted in May 2020 to target synthesized literature on croup, tracheitis and recurrent stridor for 2015 to current and limited to English. The search was executed in Ovid Medline, Embase, Cochrane Database of Systematic Reviews (CDSR) and Turning Research into Practice (TRIP) databases.

Two reviewers independently screened abstracts and included guidelines and systematic reviews that addressed optimal diagnosis, treatment, and prognosis of patients who meet pathway inclusion/exclusion criteria. One reviewer extracted data and a second reviewer quality checked the results. Differences were resolved by consensus. <If articles were added through other sources, briefly explain if they met criteria for search above, and if not, what was rationale for adding. For example, were they carried forward from prior version of pathway.>

Literature Search Results

The search retrieved 101 records. Once duplicates had been removed, we had a total of 101 records. We excluded 82 records based on titles and abstracts. We obtained the full text of the remaining 82 records and excluded 69. We included 7 studies. The flow diagram summarizes the study selection process.



Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

2020 Bibliography page 2

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