

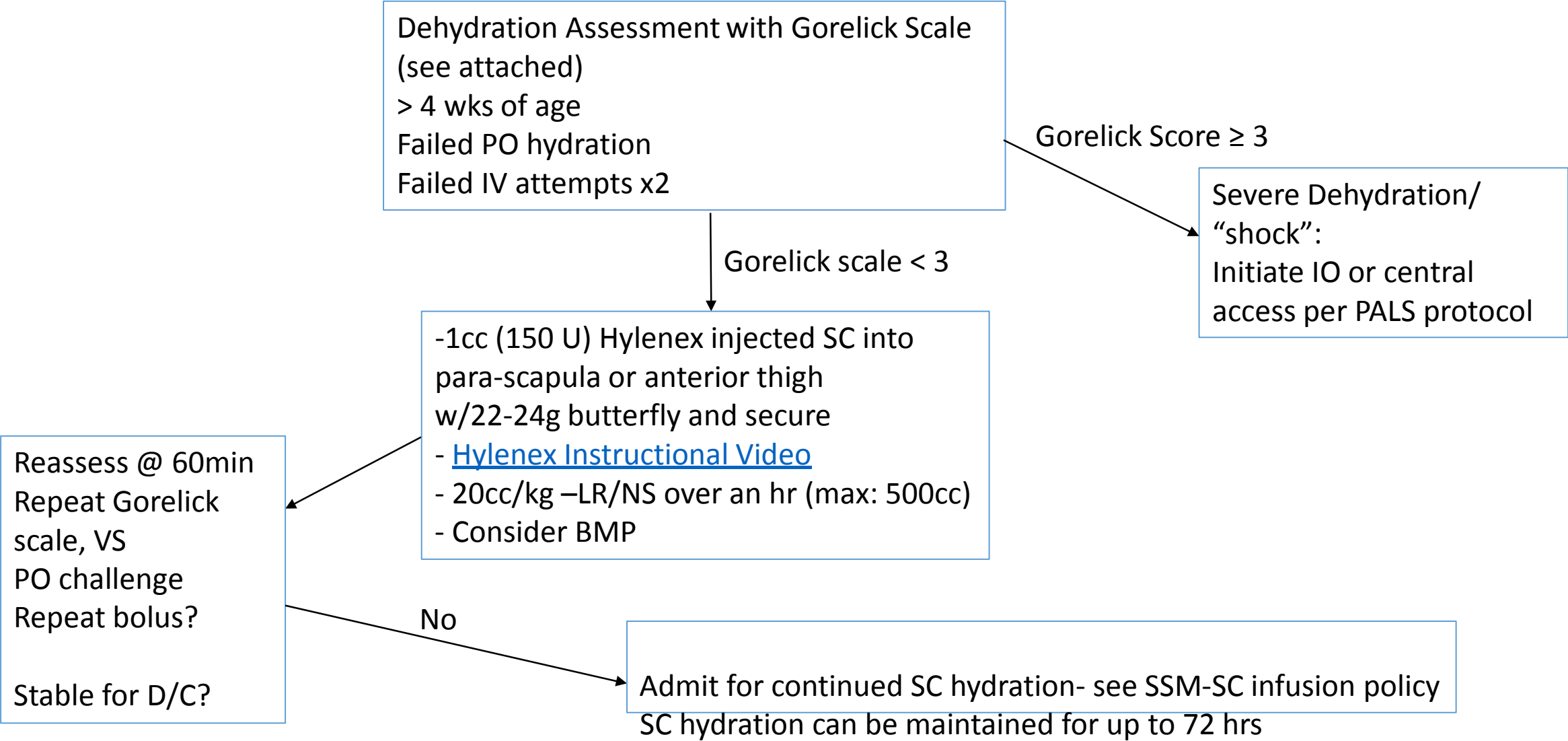
# Subcutaneous (SQ) Hydration Augmented with Hyaluronidase:

Emergency Department Management  
Clinical Practice Guideline (CPG)

Protocol approved by:  
Division of Pediatric Emergency Medicine,  
Date of approval: 1/08/15

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# Subcutaneous (SQ) Hydration Augmented by Hyaluronidase

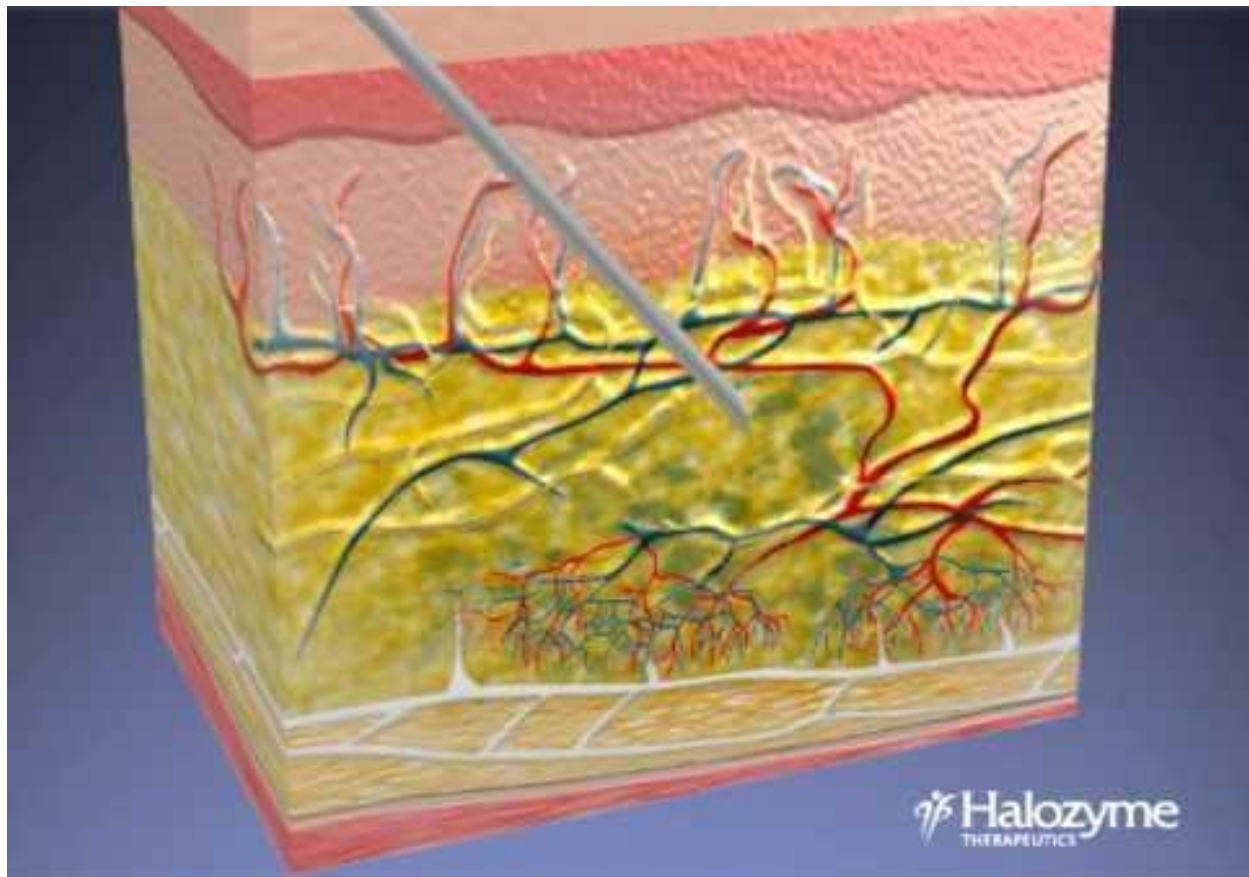


## Subcutaneous Hydration for Dehydration with Hyaluronidase

### Background:

Subcutaneous (SQ) hydration has a long track record from the early 1900's to the 1950's it was the predominate way to hydrate adults and children. A bovine derived form of hyaluronidase was utilized to breakdown the sub-cutaneous matrix to facilitate the spread and absorption of fluids.

In 2005, a recombinant human hyaluronidase (rHuPH20-Hylenex) is FDA approved for SQ fluid administration for achieving hydration in both adults and children. By catalyzing the hydrolysis of hyaluronan, a constituent of the extracellular matrix (ECM), hyaluronidase lowers the viscosity of hyaluronan, thereby increasing tissue permeability. It is used in conjunction with solutions to speed their dispersion and delivery.



Intravenous (IV) placement of catheters in children with dehydration may be difficult. Hydration through the SQ route is now a viable and effective option. Ultimately the utility of SQ hydration may be in hospitals who infrequently place IV's in children or in mass casualty/disaster situations but it's an old form of treatment being re-visited.

**The data is growing and appears that SQ hydration is an effective and patient friendly way of treating mild to moderate dehydration.** Three recent studies (1 adult and 2 children) since FDA approval have assisted in re-vitalizing the concept:

INFUSE – LR Clinical Study (1/05 – 1/06)

INFUSE – Pediatric Rehydration Study I (8/07-6/08)

INFUSE – Pediatric Rehydration Study II (11/08-12/09)

INFUSE LR– The INFused Flow Utilizing Subcutaneous-Enabled Rehydration (INFUSE I)- LR Clinical study

1st clinical study to assess safety and tolerability of rHuPH20

- Adults, two armed, blinded, placebo controlled
- SC infusion of LR with and without Hylenex 4 fold greater flow with Hylenex vs placebo
- N=36 (all adults)
- Subject-rated discomfort was lower vs placebo (5.8 vs 9.6) on VAS ( $p < .002$ )
- All AE's were localized (i.e. site discomfort, swelling)
- No severe or serious AE's

INFUSE I- The INFused Flow Utilizing Subcutaneous-Enabled Pediatric Rehydration

- Prospective, single arm, phase IV, multicenter study
- Safety, efficacy and ease of use study
- Outcome: the % of patients who achieved successful rehydration

- N=51, (2m-10 yrs.) w/mild to mod dehydration
- Most <3 yrs.
- 20cc/kg isotonic fluid Assessed the efficacy, safety and utility of Hylenex in rehydration of children with mild to moderate dehydration
- Phase IV, single arm, pilot study
- N=51, (2m -10yrs) received 1ml of Hylenex followed by 1 hr of 20cc/kg of isotonic fluids
- Endpoint: Proportion of patients successfully rehydrated by SQ infusion and discharged without the need for further rehydration
- Secondary: ease of use, time to catheter placement number of attempts needed and AE's
- 100% successful SQ placement
- 94% (48/51) were clinically rehydrated via SQ
- Median time to infusion after catheter placement: 2min (range 0-15min)
- 90% only required 1 attempt
- 10% dislodged and required reinsertion
- Investigators rated SQ as more effective (92%) and less difficult (90%) than IV infusion
- 90% parents rated satisfied or very satisfied with the procedure; 94% considered the procedure a success

### INFUSE II - The INFused Flow Utilizing Subcutaneous-Enabled Pediatric Rehydration (INFUSE II)

Prospective, 2 –arm, phase IV trial, multicenter, open label, randomized, non-inferiority study:

- To evaluate Hylenex augmented enabled SQ fluid administration can be given safely and effectively, with volumes similar to those delivered IV, in children with mild to moderate dehydration

- Total mean volume of hydration fluid infused at a single site (ED plus inpatient)
- Dehydration defined via Gorelick scale (see attached)
- N=148
- Age (>1m to 10 yrs)
- 20cc/Kg Isotonic fluid after 150ug Hylenex SC
- Non-inferiority study powered to test the mean volume infused via SQ was >85% of the volume delivered by IV
- N=74 per group would provide at least 80% power for establishing the non-inferiority of Hylenex SQ vs IV
- 95% vs 74.6% Needle placement after 1 stick
- 21% failed IV placement and were “rescued” by SQ
- 100% SQ success across all age groups, 5% required a 2<sup>nd</sup> stick
- 93% of ED patients were successfully hydrated SQ vs 88% in the IV treatment arm
- Mean rate of fluid administration (20cc/kg/hr) similar for SQ vs IV
- Mean ED total volume delivered was similar (406cc SQ vs 413cc IV)
- Erythema: 54% SQ vs 19% IV
- Pain: 78% vs 59%
- Edema: 5% vs 1%
- All were considered mild to moderate in severity
- No SAE’s were reported

This clinical practice guideline, including a copy of Gorelick’s dehydration scale and a link to a video demonstrating how Hylenex is administered, is available on the Cardinal Glennon Web site.

## References:

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- Coburn HA, Etwiler LS, Miller MK. et al. Recombinant human hyaluronidase enabled subcutaneous pediatric rehydration. *Pediatrics* 2009;124:e859-e868
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# Dehydration Assessment

(adapted from Cortick Mal')

*"The essential first step to timely and appropriate management of your pediatric patients"*

— M. atc Genttic, MQ, MSCF

Simply check  abnormalities that apply and total the number of checks:



Abnormal general appearance



Capillary refill > 2 seconds



Dry mucous membranes



Absent tears

Total checks \_\_\_\_\_

This scale is one of several tools to be considered in treatment decisions. Consult your institution's policy and procedures.

This assessment includes the four most common predictive signs or symptoms from the 10-criterion Gordick scale: general appearance, capillary refill > 2 seconds, absence of tears, and dry mucous membranes. The remaining criterion assessed include decreased skin elasticity, abnormal respirations, sunken eyes, abnormal radial pulse, tachycardia (HR > 150), and decreased urine output.

## CLINICAL DEHYDRATION SCORE:

0 = No dehydration

1 = Mild dehydration (< 5%\*)

2 = Moderate dehydration (5%-9%\*)

≥ 3 = Severe dehydration (≥ 10%\*)

†Gordick MW, Sitawon K, Murphy KO. "The 10-criterion Gordick scale." *Pediatrics* 1991;87:1011-1014.

\*Approximate percent of total body weight lost to dehydration.



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