Julie Weiner, DO

Dr. Weiner is one of the neonatologists at Children's Mercy and is currently the Medical Director of the level IV NICU. She is a native of Kansas City and has 3 boys (2 in college at Oklahoma University and 1 that is a Junior in High School). In June, it will be she and her husband's 25th wedding anniversary.

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Mystery Case

Julie Weiner, DO
Attending Neonatologist
Medical Director CMH NICU

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Disclosure Statement

- I have no actual or potential conflict of interest in relation to this program

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Objectives

- Know the Differential Diagnosis for Neonatal Skin Lesions
- Describe the testing to achieve the diagnosis
- Understand unique care needs for rare neonatal congenital skin defect

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Mystery Case: Baby J

- Called for Transfer:
  - Male infant who is 38 5/7 weeks, 2.532 Kg
  - Mom is 26 yo G2P2
    - Prenatal labs: O+, GBS neg, Rubella Immune, Hep B neg, HIV neg
    - Hx of pre-eclampsia, prolactinoma
    - ROM 5 hrs, APGARs 9 and 9 at 1 and 5 mins

- **Delivery management**
  - Routine warmth, drying, clearing airway and stimulation.
  - Medications given: Vitamin K, erythromycin ophthalmic.
  - Summary of events: Called at 4 min of life due to skin breakdown at the upper and lower extremities joints.

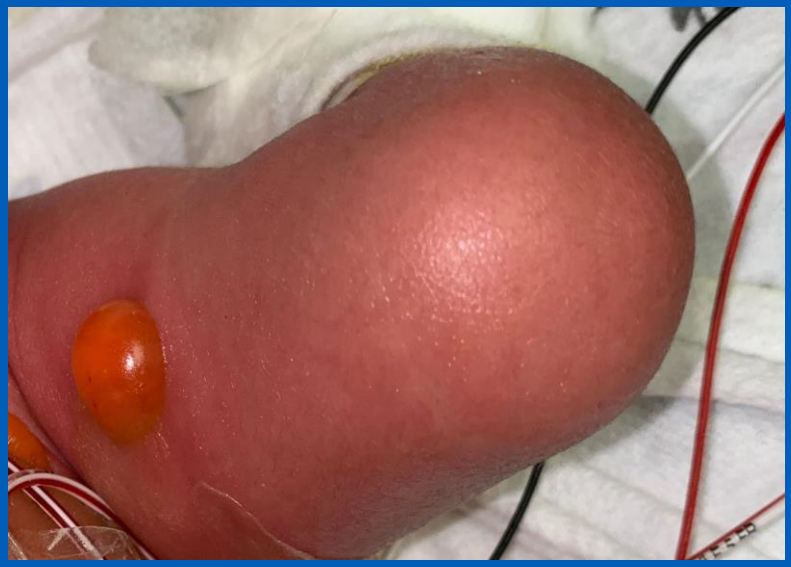
Transport

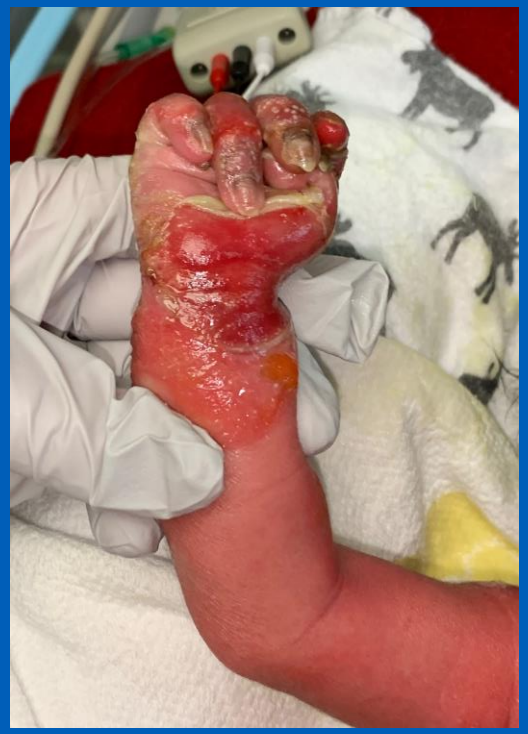
- NPO
  - Started on IV Fluids
- Room air
- Pain control
  - PRN Morphine
- Antibiotic Coverage
  - Ampicillin and Gentamicin

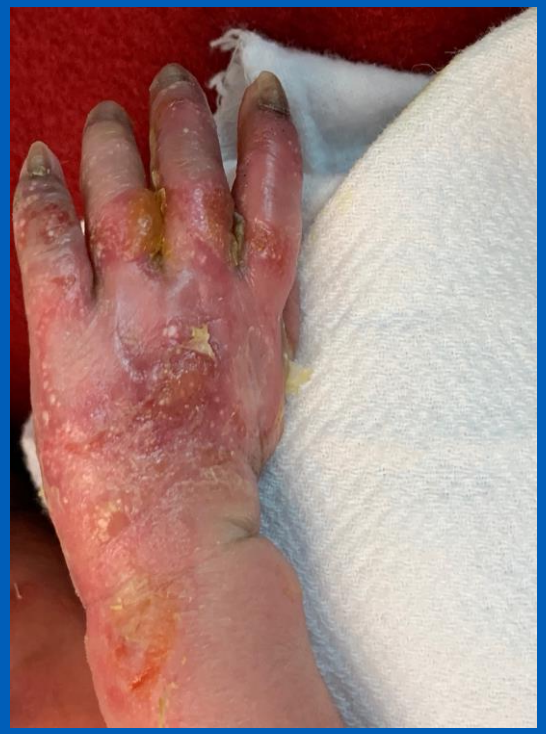
Baby J

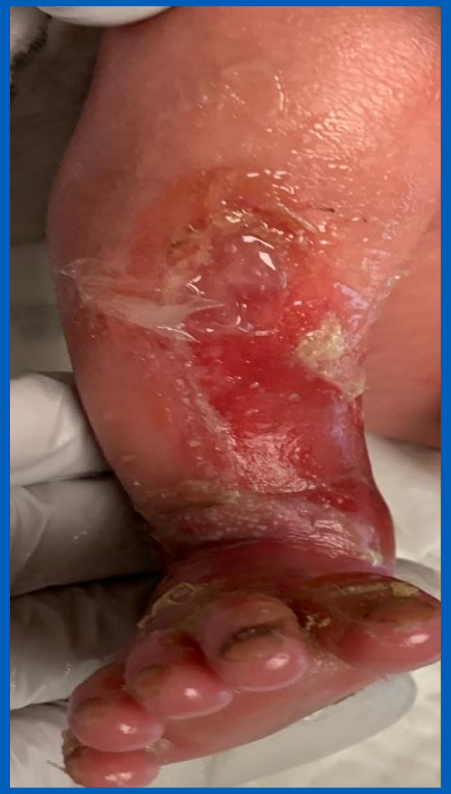
- Skin
  - Multiple areas of denuded skin around the distal joints (wrist and ankles)
  - Areas are red and tender with overlying sloughing.
  - After admission multiple new bullae appeared

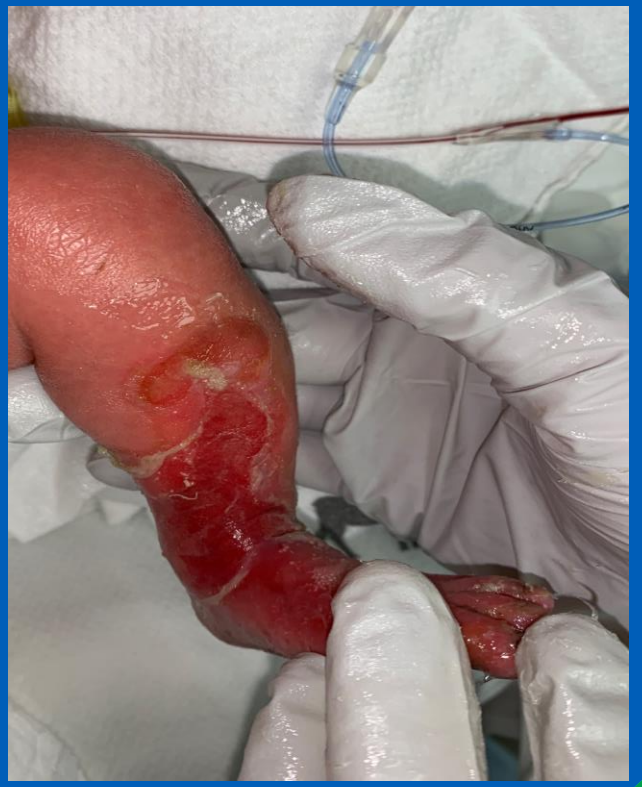
Skin Findings on Admission











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What is your working diagnosis?

Infectious - Viral (ex. HSV) 0%

Infectious - Bacterial (ex. Staph Scalded Skin) 0%

Congenital Skin difference 0%

Trauma 0%

Autoimmune response (ex. Neonatal lupus) 0%

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Differential Diagnosis

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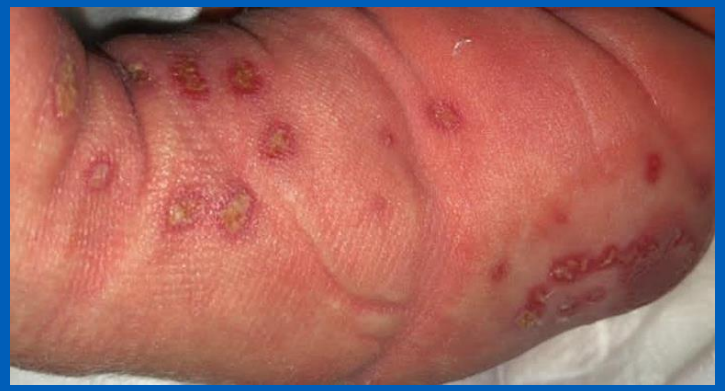
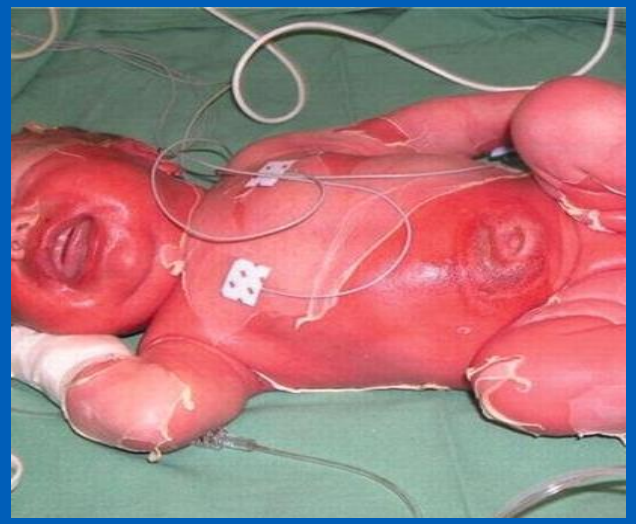
Differential Diagnosis

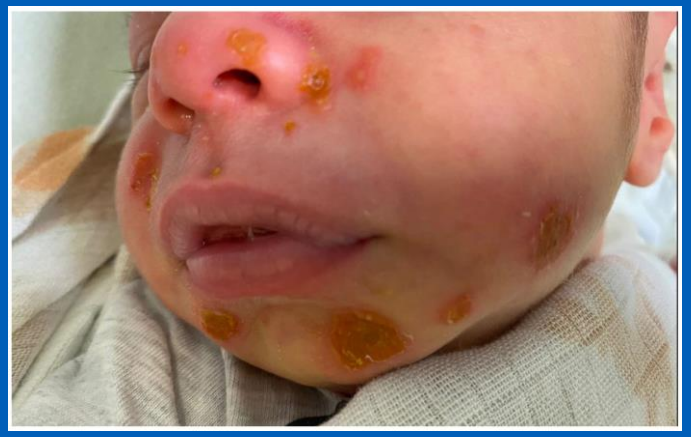
- Infectious
  - HSV



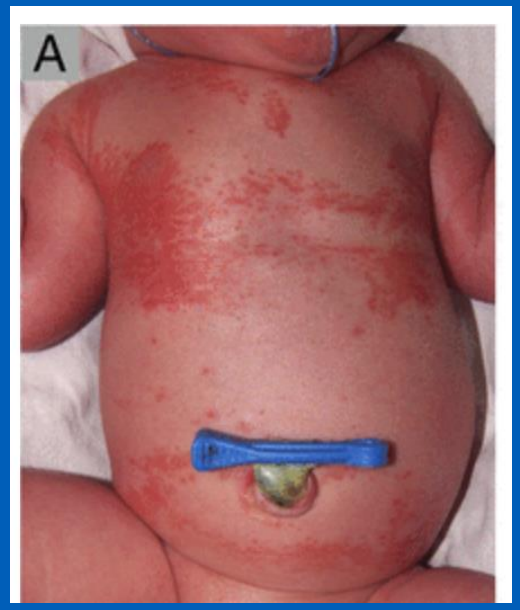
  - Staphylococcal Scalded Skin Syndrome



Bullous Impetigo



Neonatal Candidiasis



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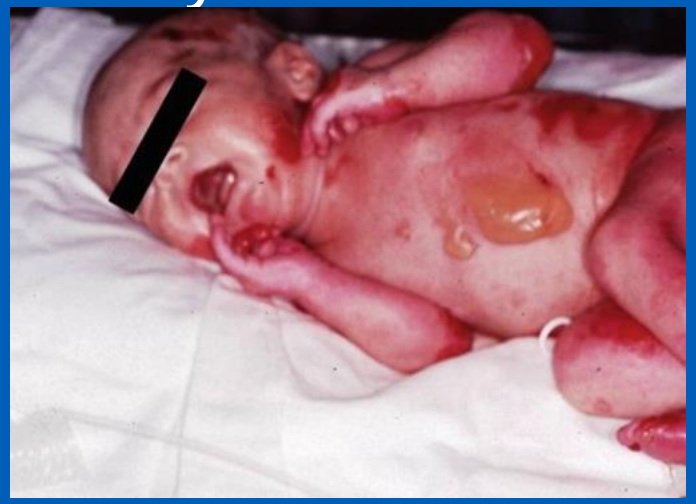
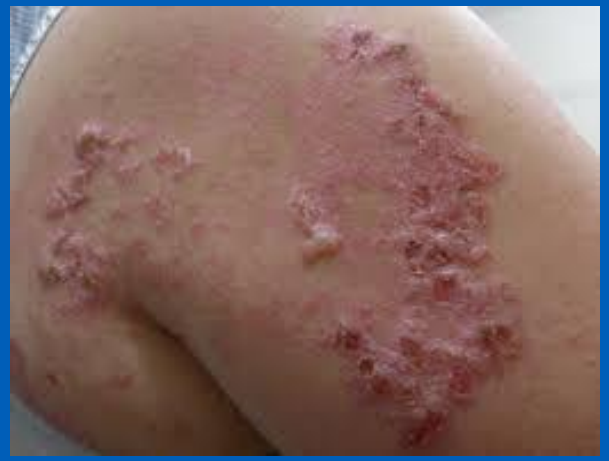
Congenital Skin Conditions

Epidermolysis Bullos

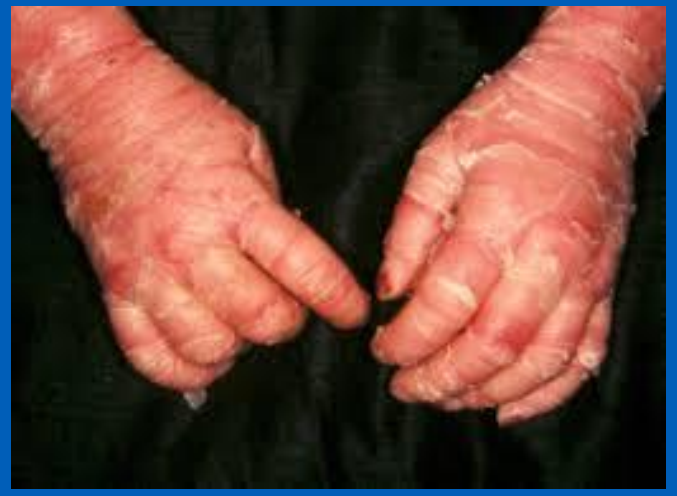


Incontinentia pigmenti

Blistering Genodermatose



Epidermolytic ichthyosis



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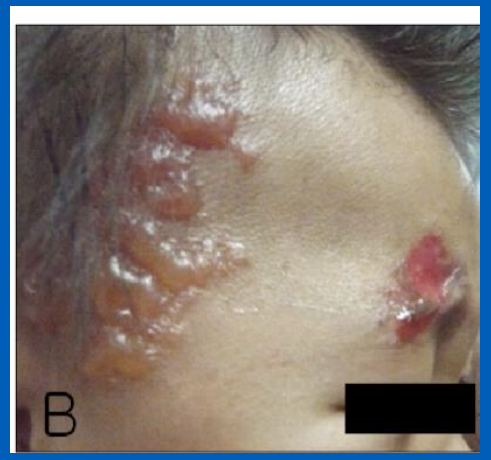
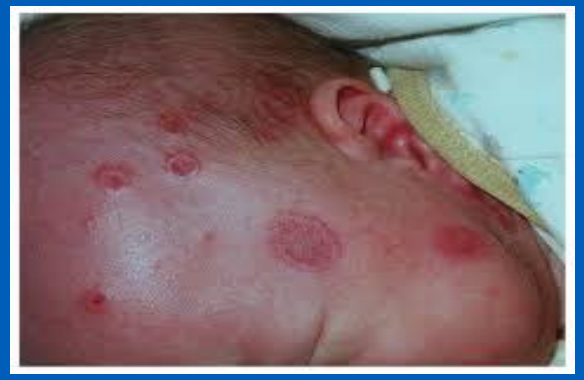
Other

Bullous Mastocytosis

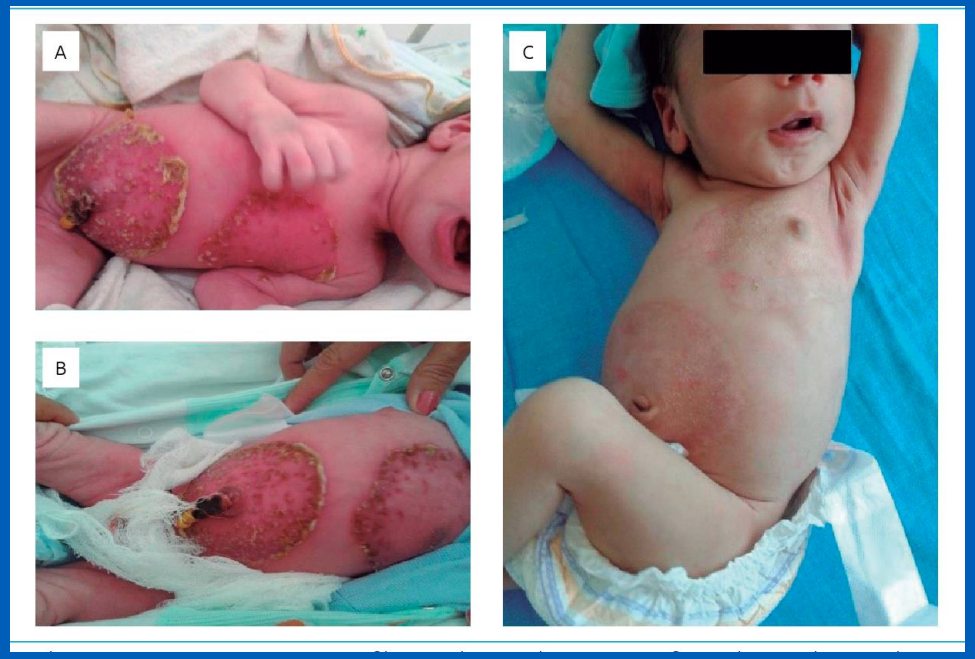


Neonatal Lupus



Mothers with Autoimmune conditions

- Neonatal pemphigus and pemphigoid



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Testing

- Infectious concerns
  - Cultures of the skin lesion (viral, bacterial, fungal cultures)
  - Blood cultures and/or PCR
- Congenital Skin differences
  - Genetic Testing
    - Blood, saliva or tissue
    - NGS-targeted gene panels
      - ~1 month turn around time
    - Whole-exome sequencing
      - More expensive
      - May identify novel genes with mutations missed by NGS
    - Whole genome sequencing and Ultra-rapid targeted genomic sequencing
      - Newer, can be used to screen over ~1700 genes, results in ~3 days
  - Skin Biopsy

Baby J's Diagnosis

- Suspected a form of Epidermolysis Bullosa
  - Derm was consulted
  - Genetic Studies sent
    - Next-Generation Sequencing
- Epidermolysis bullosa (EB)
  - 1 in 8.2 million live births in the US
  - Classifications were updated in 2020
    - More based on genetics rather than clinical features
    - 16 genes associated with classical types of EB
      - EB simplex
      - Junctional EB
      - Dystrophic EB
      - Kindler EB

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Molecular and Genetic Classifications of EB

Table 1. Molecular and Genetic Classification of EB

Type	Inheritance	Gene	Protein
EB simplex (Intra-epidermal)	Autosomal dominant	*KRT5*	Keratin 5
		KRT14	Keratin 14
		PLEC	Plectin
		KLHL24	Kelch-like protein 24
	Autosomal recessive	*KRT5*	Keratin 5
		KRT14	Keratin 14
		DST	BP230 (BPAG1e, dystonin)
		EXPH5 (SLAC2B)	Exophilin-5 (synaptotagmin-like protein, homolog lacking C2 domains b, Slac 2b)
		CD151 (TSPAN24)	CD151 antigen (tetraspanin 24)
Junctional EB (junctional)	Autosomal recessive	*LAMA3, LAMB3, LAMC2*	Laminin 332
		COL17A1	Type XVII collagen
		ITGA6, ITGB4	Integrin α6β4
		ITGA3	Integrin α3 subunit
Dystrophic EB (dermal)	Autosomal dominant	*COL7A1*	Type VII collagen
	Autosomal recessive	*COL7A1*	Type VII collagen
Kindler EB (mixed)	Mixed	*FERMT1 (KIND1)*	Fermitin family homolog 1 (Kindlin-1)

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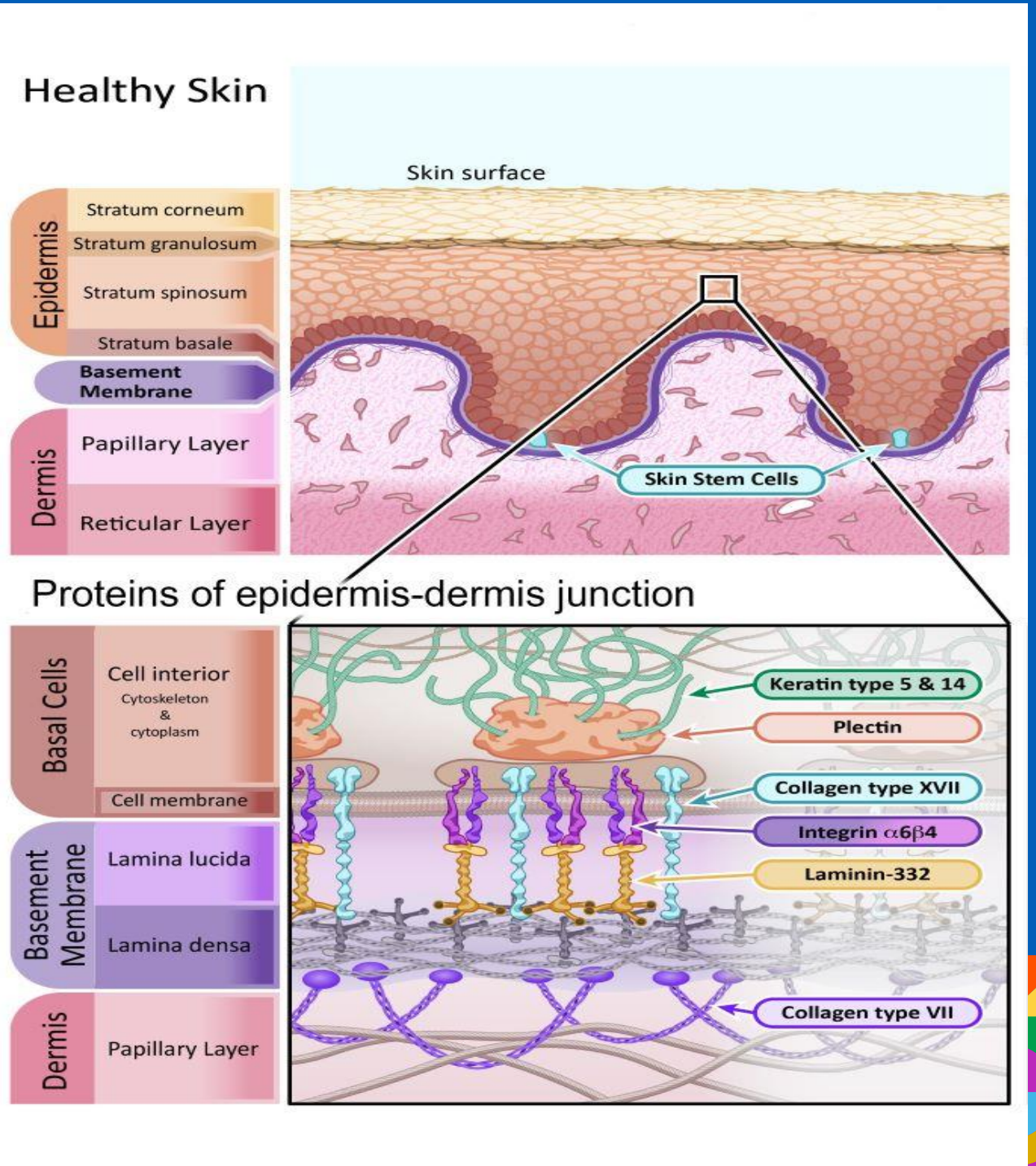
Lucky, A. et. Al. Diagnosis and care of the Newborn with Epidermolysis Bullosa. *Neoreviews*(2021)22(7): e438-e451

Classifications of EB

- EB simplex (EBS): Proteins located in the epidermis
- Junctional EB (JEB): Proteins located in the basement membrane between the epidermis and dermis
- Dystrophic EB (DEB): Located in the anchoring fibrils of the dermis
- Kindler EB: Located in several layers of the skin



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Why the Diagnosis Matters

- Prognostication
  - Lethal forms
  - Other associated congenital anomalies
    - Pyloric atresia, Renal abnormalities,
  - Wide range of long-term complications

- Reoccurrence Risk
  - De Novo mutation vs. Inherited

Baby J's Diagnosis

- Genetic report:
  - Krt14 pathogenic variant- with variable severity, basal cleavage.
  - Affects Keratin 14 protein
  - Autosomal Dominant

Differential Diagnosis

- Clinical:
  - range in severity (some reported deaths in neonatal due to sepsis, improvement with age). blistering can occur-hands/feet,arms, oral blistering with clusters.
- De Novo random genetic change, he did not inherit this from either parent.

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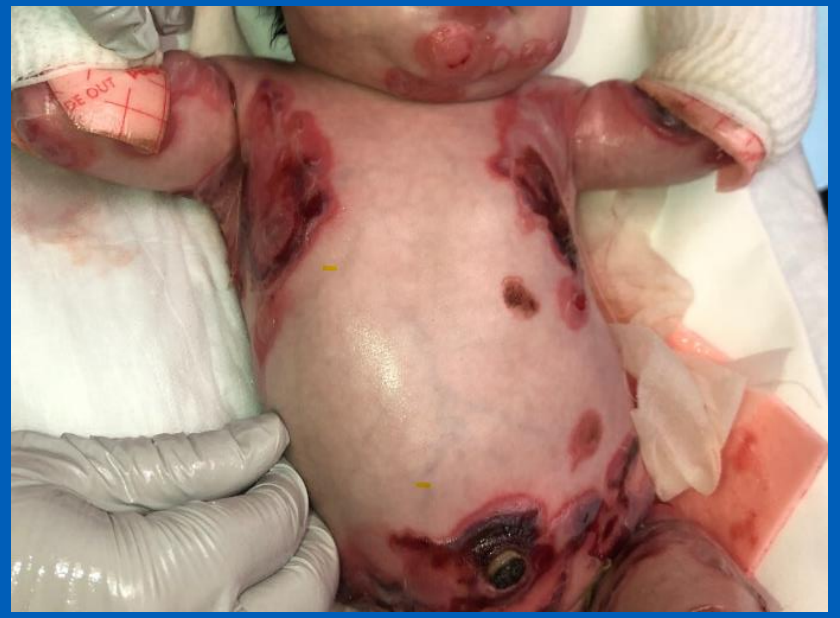
Unique Care Considerations

- Minimizing friction/rubbing of the skin as much as possible as this may induce new blister formation.
- General Assessments:
  - Vitals
    - Spot check Pulse ox, no monitor leads
  - Handling and Physical assessment
    - Containment/Swaddling
    - Diapers
      - Elastic cut out, liner/barrier, lubricated
      - No wipes, cotton balls/gauze
    - Physical Exam
  - Environment
    - Bed
      - Z-flo mattresses, sheepskin, air mattresses



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Unique Care Requirements

- Thermoregulation
  - Evaporative Losses
  - Temperature regulation
    - Heat can cause blistering
- Nutrition
  - IV placement and securement
  - Feeding
    - Enteral and Oral feeding
- Pain Control
  - Pain control (balancing respiratory depression)
- Infections
  - Topical and systemic antibiotics as needed
  - Surveillance cultures as needed
- Respiratory
  - Airway compromise can be life-threatening
  - Stridor, hoarse or weak cry

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Hospital Course

- Baby J was in the NICU for 3 months
- Skin Care
- Nutrition
- Complicated by:
  - Anemia
  - Airway Concerns
  - Scaring
  - Infection
  - Pain control
- Getting ready for home

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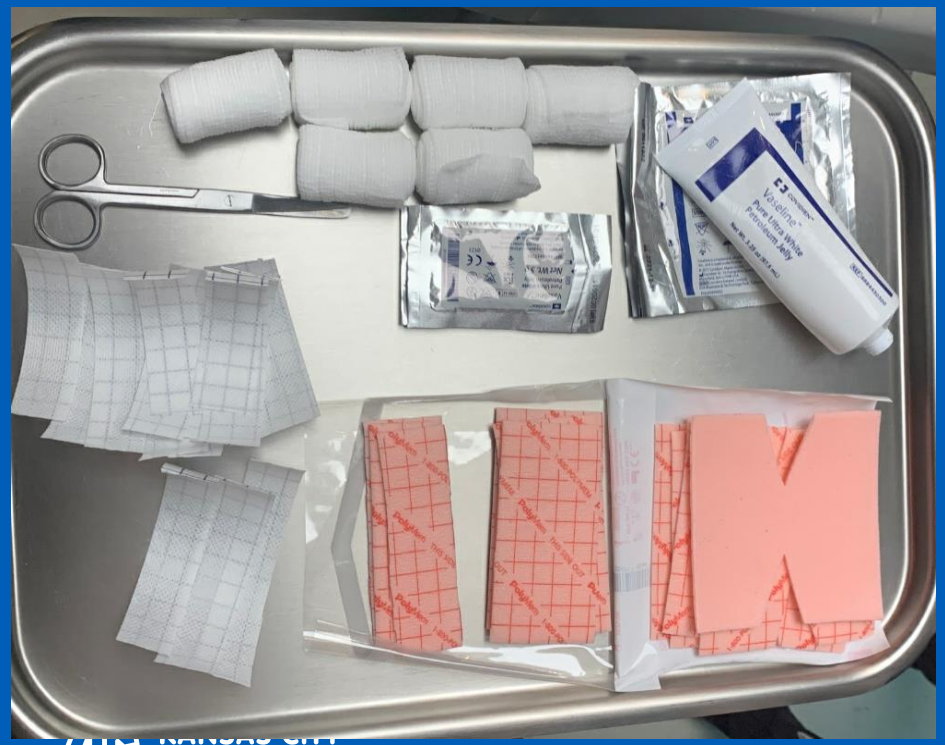
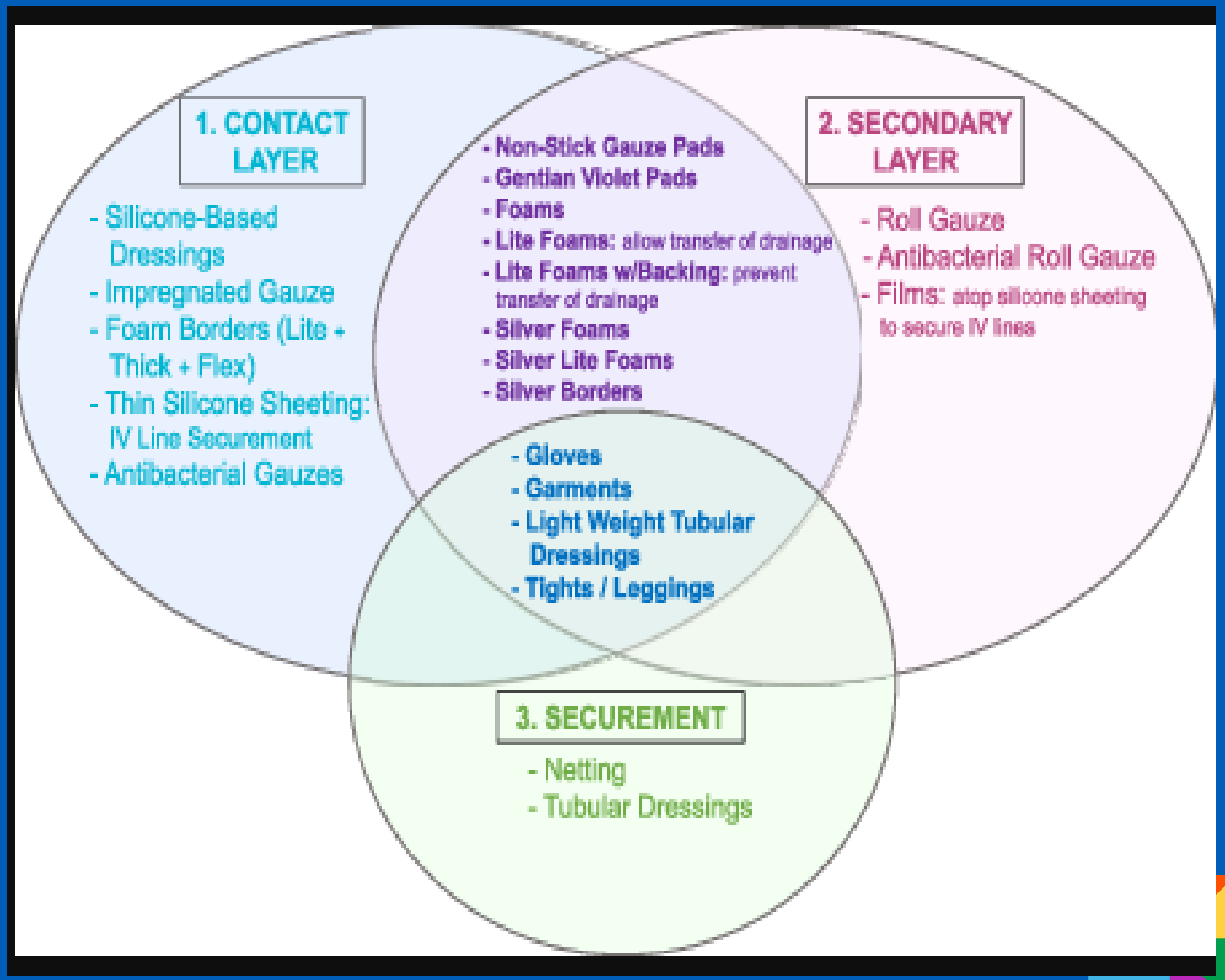
Skin Care

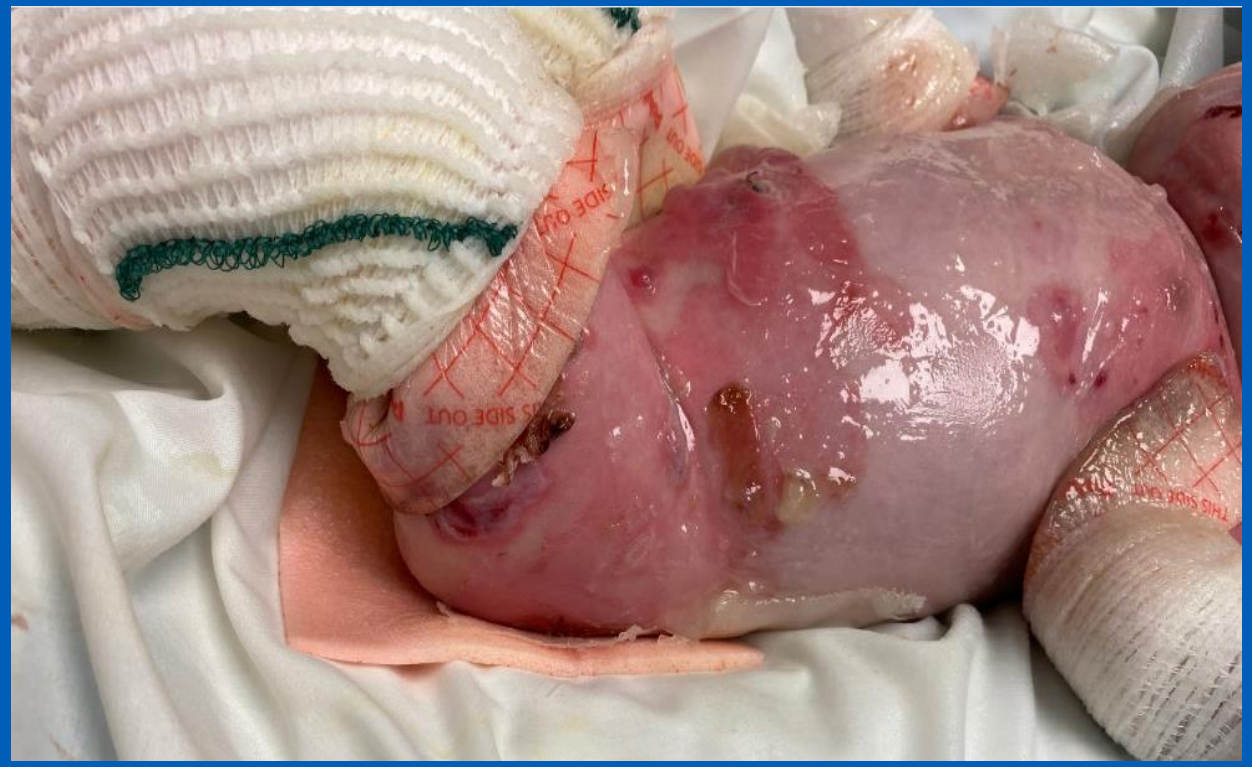
- 3 main components:
  - Contact layer
  - Secondary Laer
  - Securement of dressing





Skin Care Cont.

- Emollients used first
  - Place on contact layer, not directly on skin
  - Aquaphor, petrolatum, others
- Blisters of at least 5mm should be lanced and drained
- Topical antibiotics as needed
  - Avoid overuse
  - Bacitracin, Polysporin
  - Medical Grade Honey
  - Prescription strength topical antibiotics may be needed
    - Gentamicin, silver products, mupirocin



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Skin Care Cont

Dressing Changes every other day

- Best if 1 limb at a time
- Sponge Bath, rinse with syringe
- Work up to tub bath

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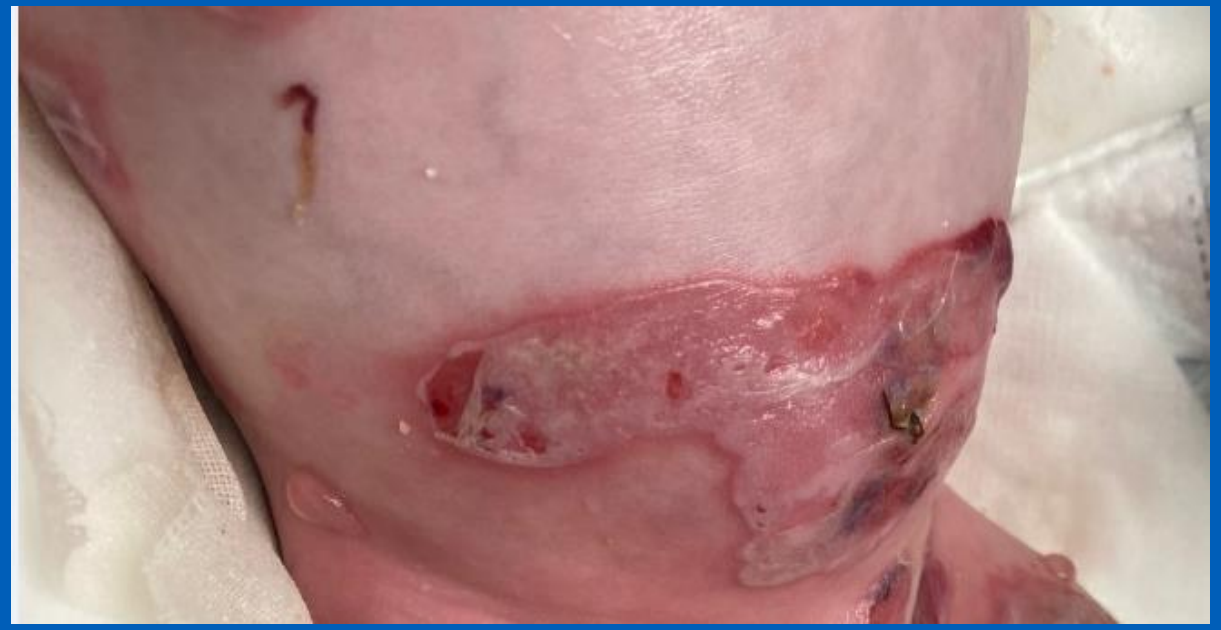
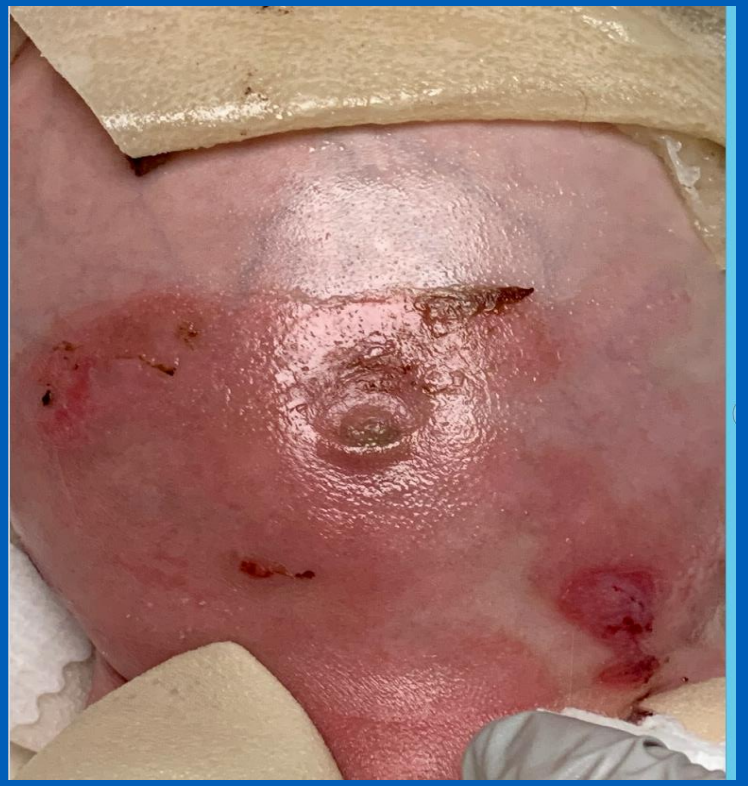
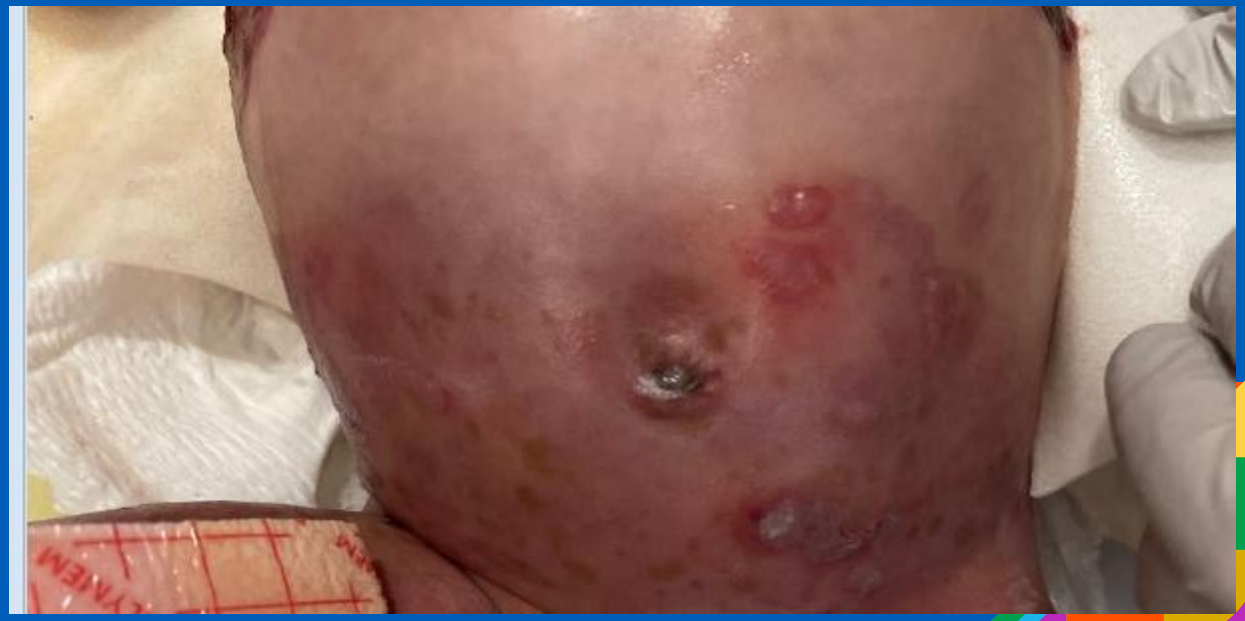
Skin Care cont







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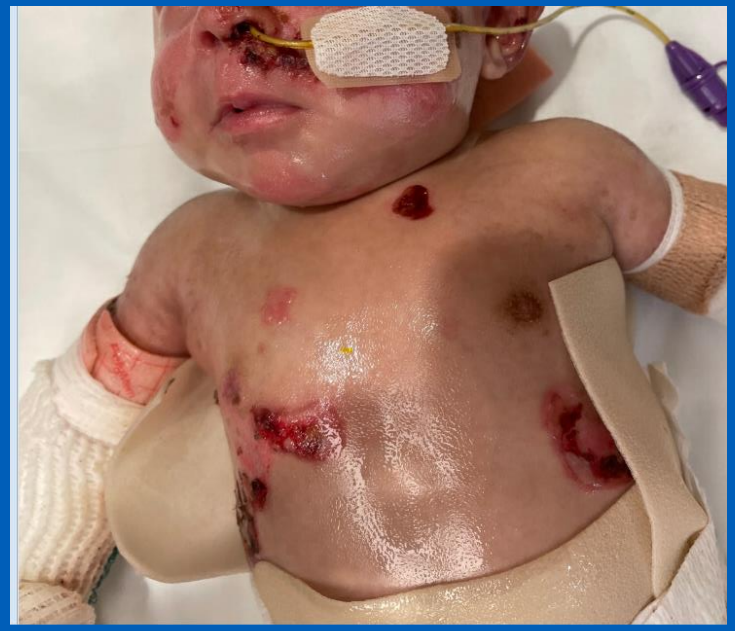
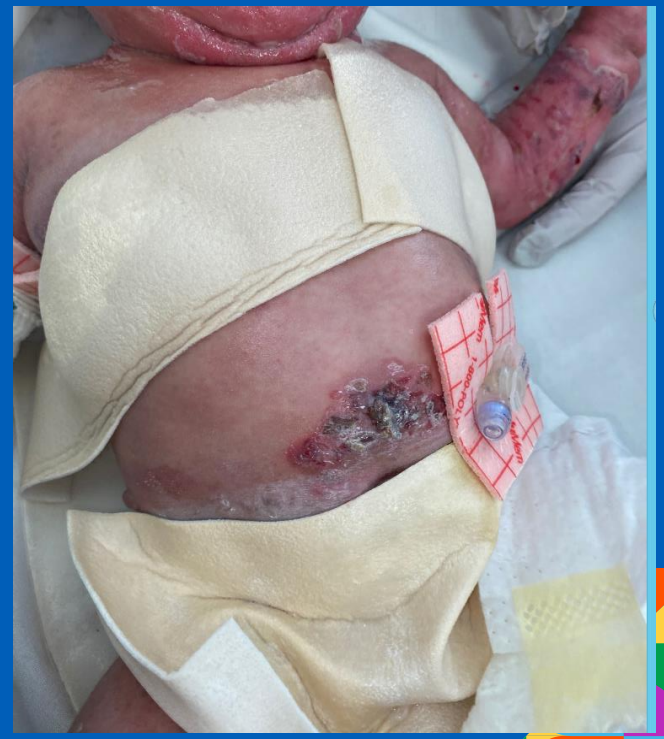
Nutrition

- IV access
  - Securing to the skin
    - Nonadherent thin pad
      - Slicone-based (Mepiform)
- Nutritional deficits
  - Low protein
  - Low zinc
- Enteral feeds
  - Oral Blisters and erosions
  - Pain
    - Magic mouth wash
    - Sucralfate
  - Long Term esophageal strictures
  - Bottle feeds
    - Special Feeder, Haberman nipple
  - NG feeds
    - Irritation to skin and airway
  - Gastrostomy Tube feeds





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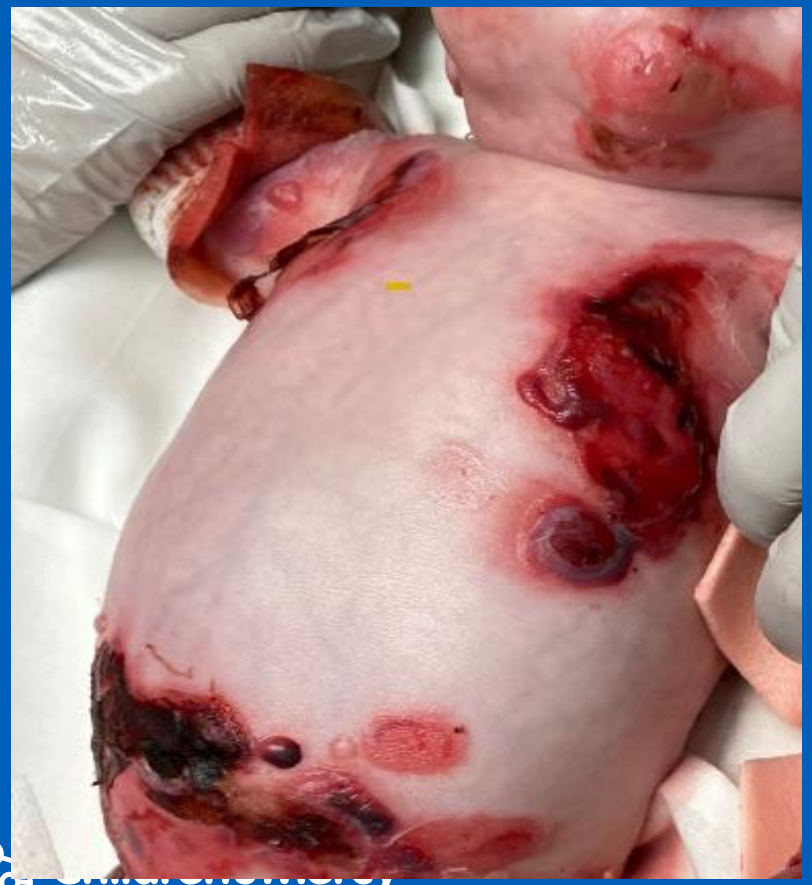
Anemia



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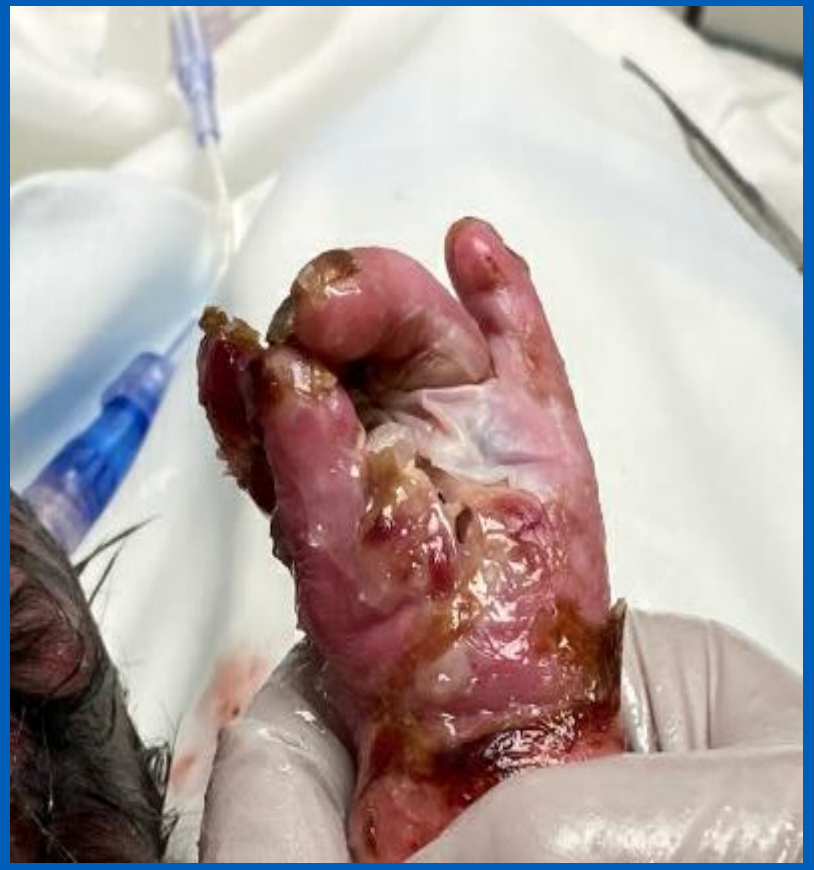
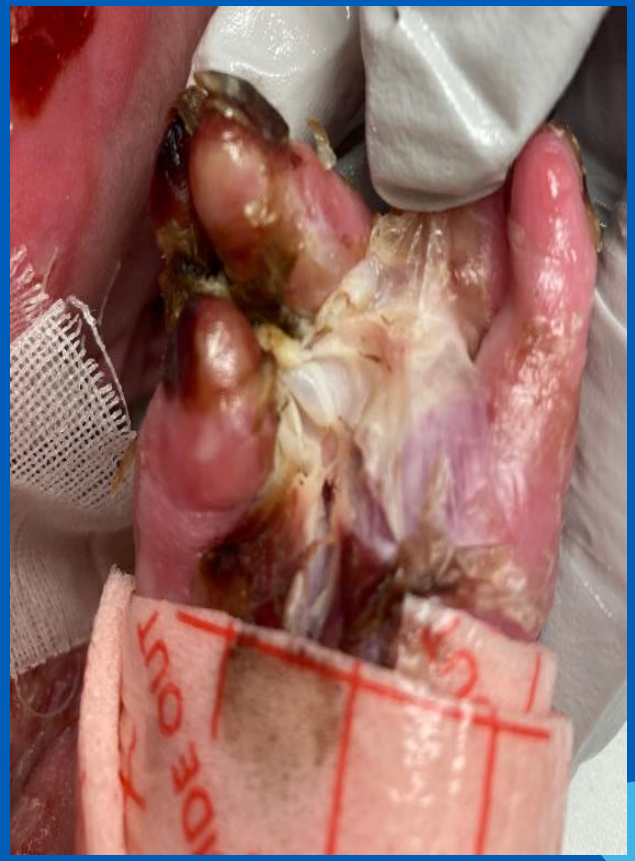
Scarring





Infections

- Extensive colonic NEC
  - 14 days of abx
  - Required Elecare feeds

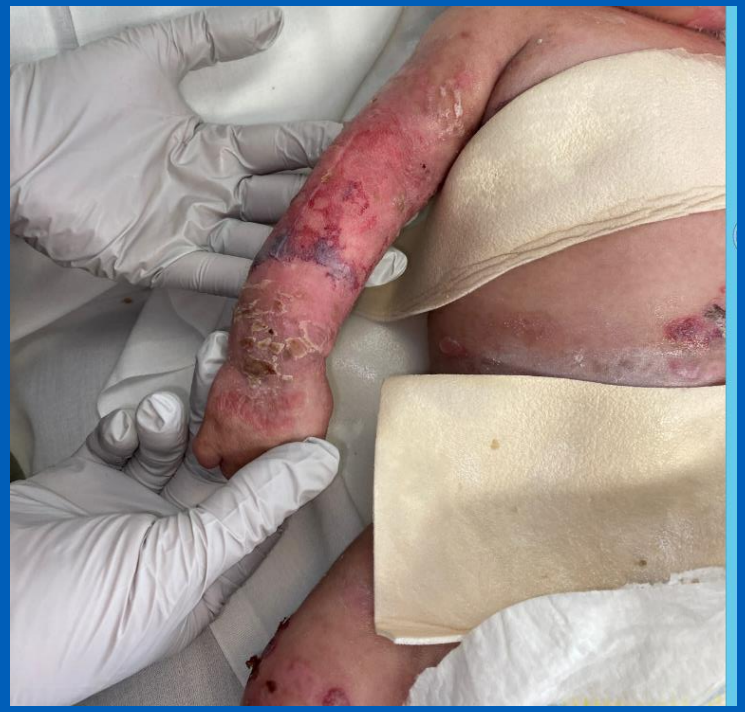
- Hx of MSSA skin cultures
- Shoulder swelling, XR images showed bony changes consistent with osteomyelitis
  - 4 weeks of abx
- Hx of wound culture of pustules on foot + for E. Coli
  - 10 days of abx
- Surveillance would cultures prn
  - Topical mupirocin and gentamicin applied as needed

Pain Control

- Morphine drip and bolus
- Tylenol prn
- Magic Mouthwash for oral sores
- Scheduled Methadone and Ativan
  - Was able to wean off prior to discharge
- Gabapentin and Clonidine
  - Discharged home on these to complete weaning schedule

Going Home

- Skin Care at home
  - $2-5K a month
  - EB Foundation
  - Wound Care Program
- Bedding
- Car Seat
- Cloths
  - Inside out, no seams
- Follow-up



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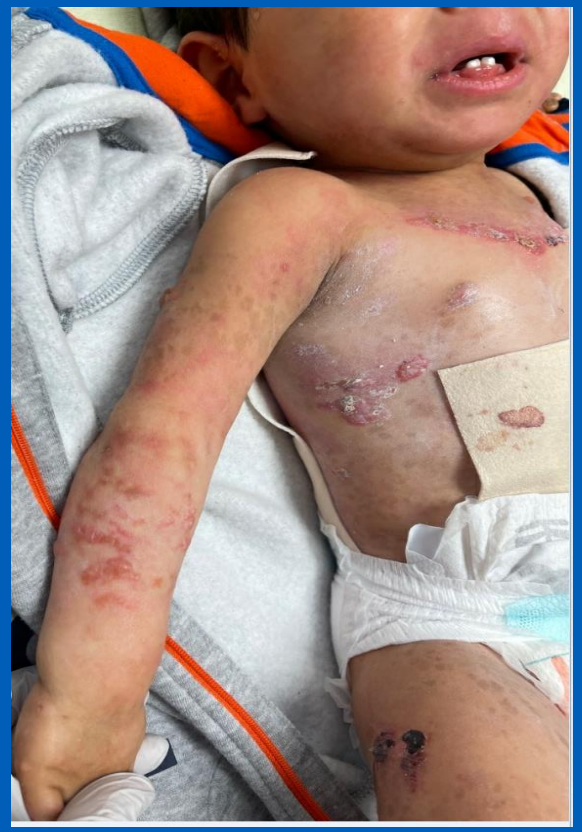
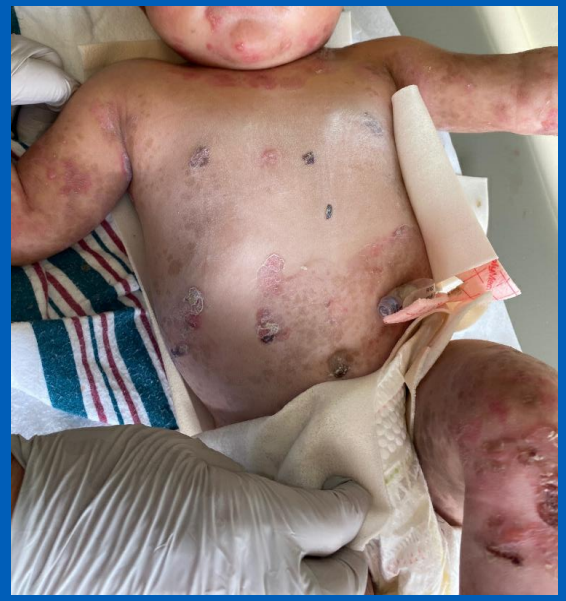
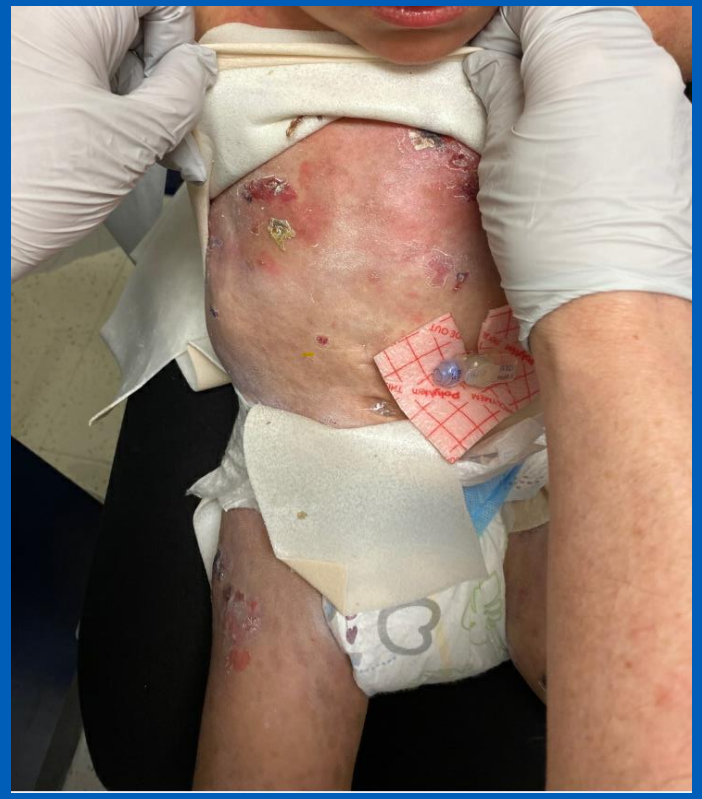
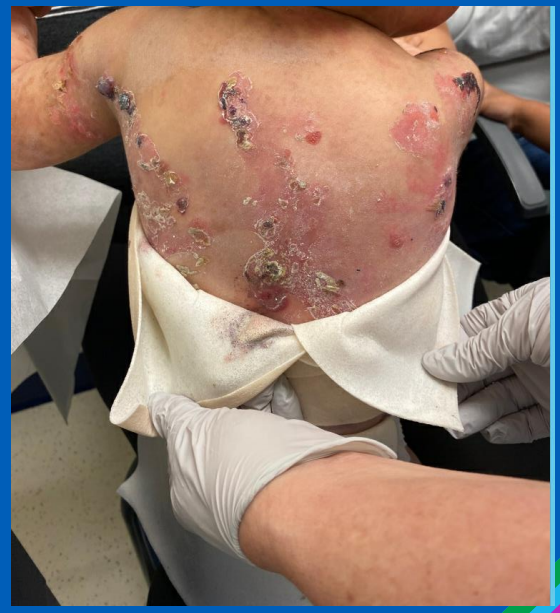
Lifelong Needs









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Questions/Discussion

- References:
- Lucky, A. et. Al. Diagnosis and care of the Newborn with Epidermolysis Bullosa. *Neoreviews*(2021)22(7): e438-e451
- Lewis, R. Epidermolysis bullosa: How Could Gene and Cell Therapy Help? Eurogct.org
- Lucky AW, Dagaonkar N, Lammers K, Husami A, Kissell D, Zhang K. A comprehensive next-generation sequencing assay for the diagnosis of epidermolysis bullosa. Pediatr Dermatol. 2018;35(2):188–197

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