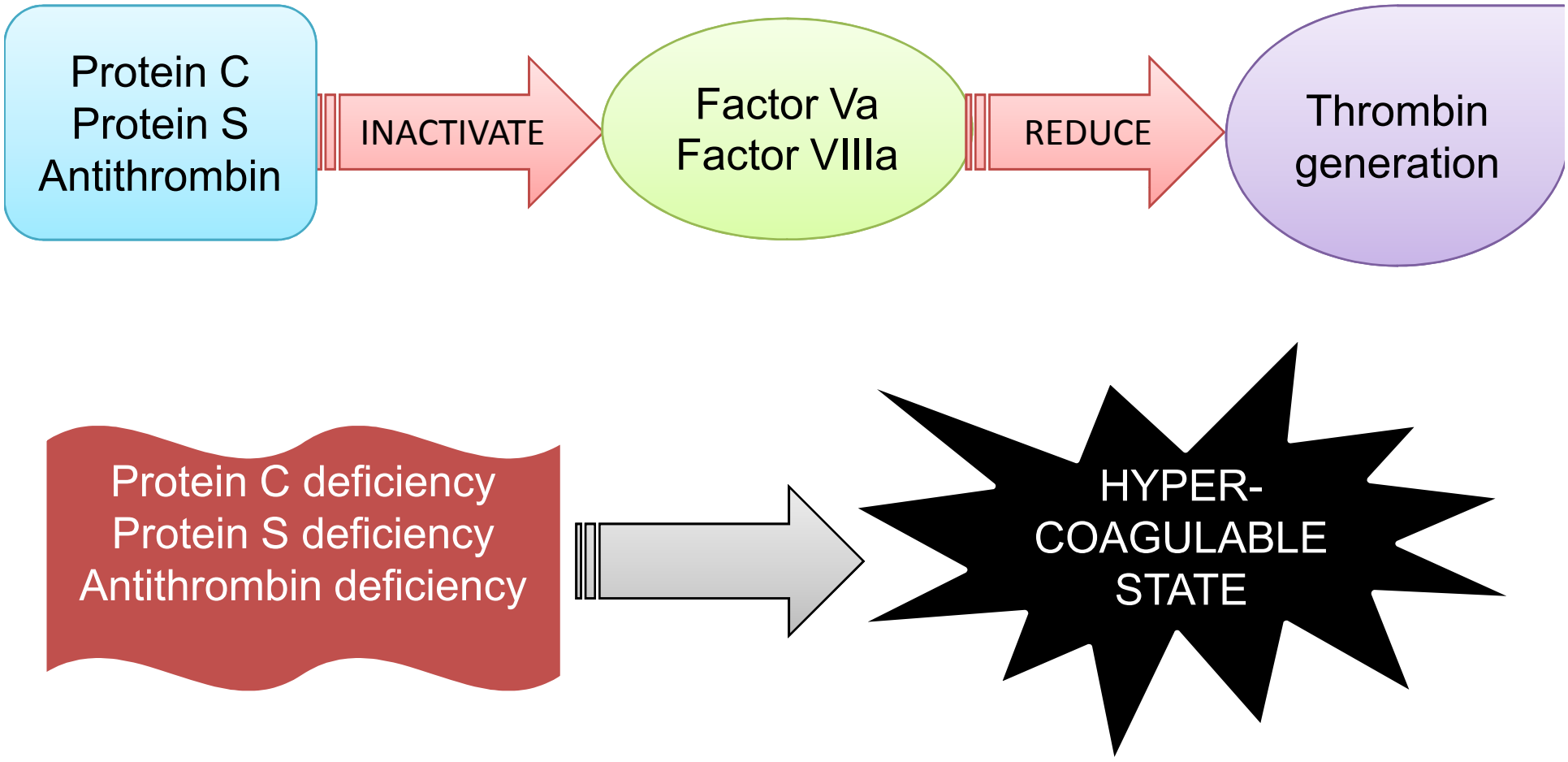
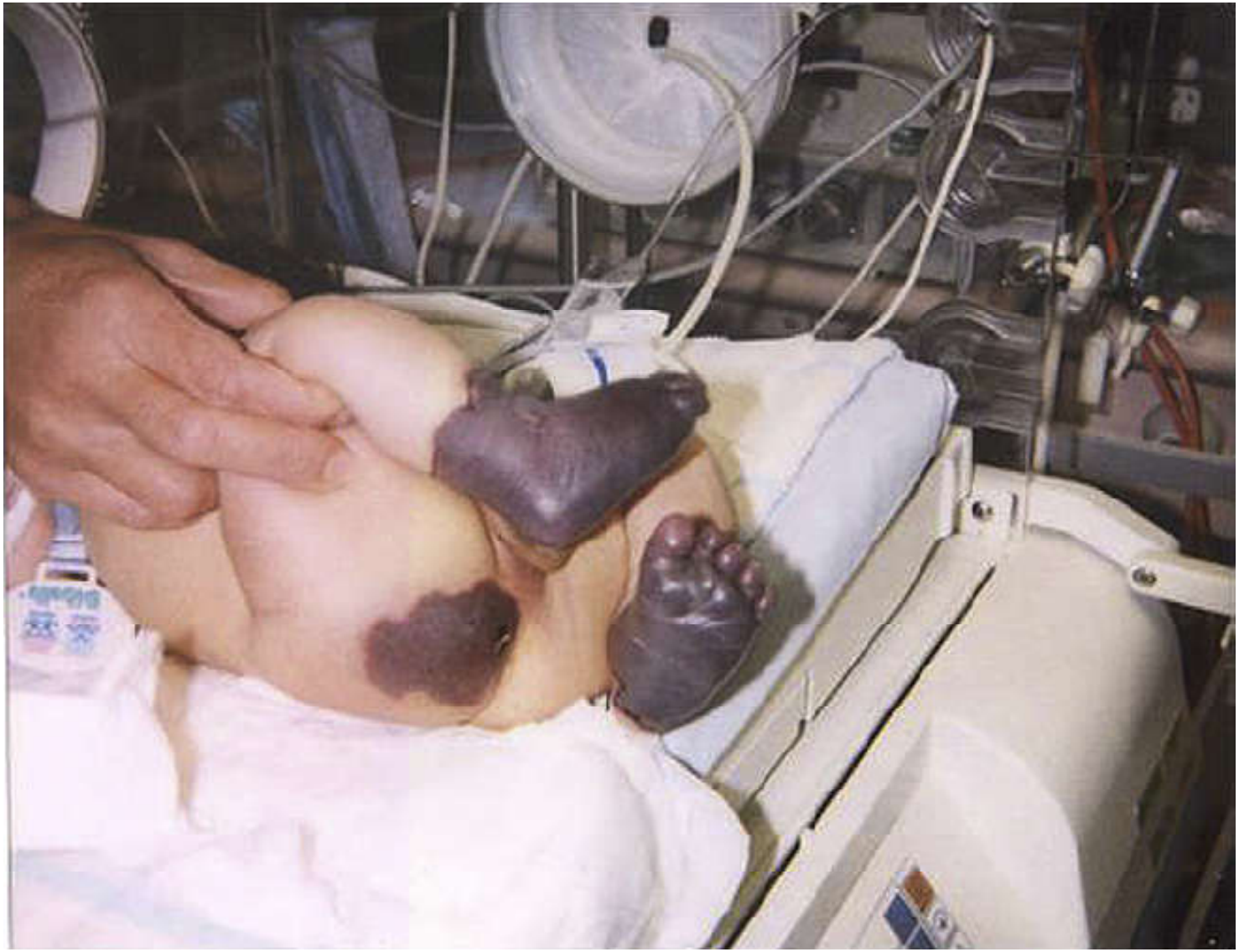
Recommedations for Management of Neonatal Purpura Fulminans

Hematology and Oncology Department
Children Hospital 2

Neonatal Purpura Fulminans

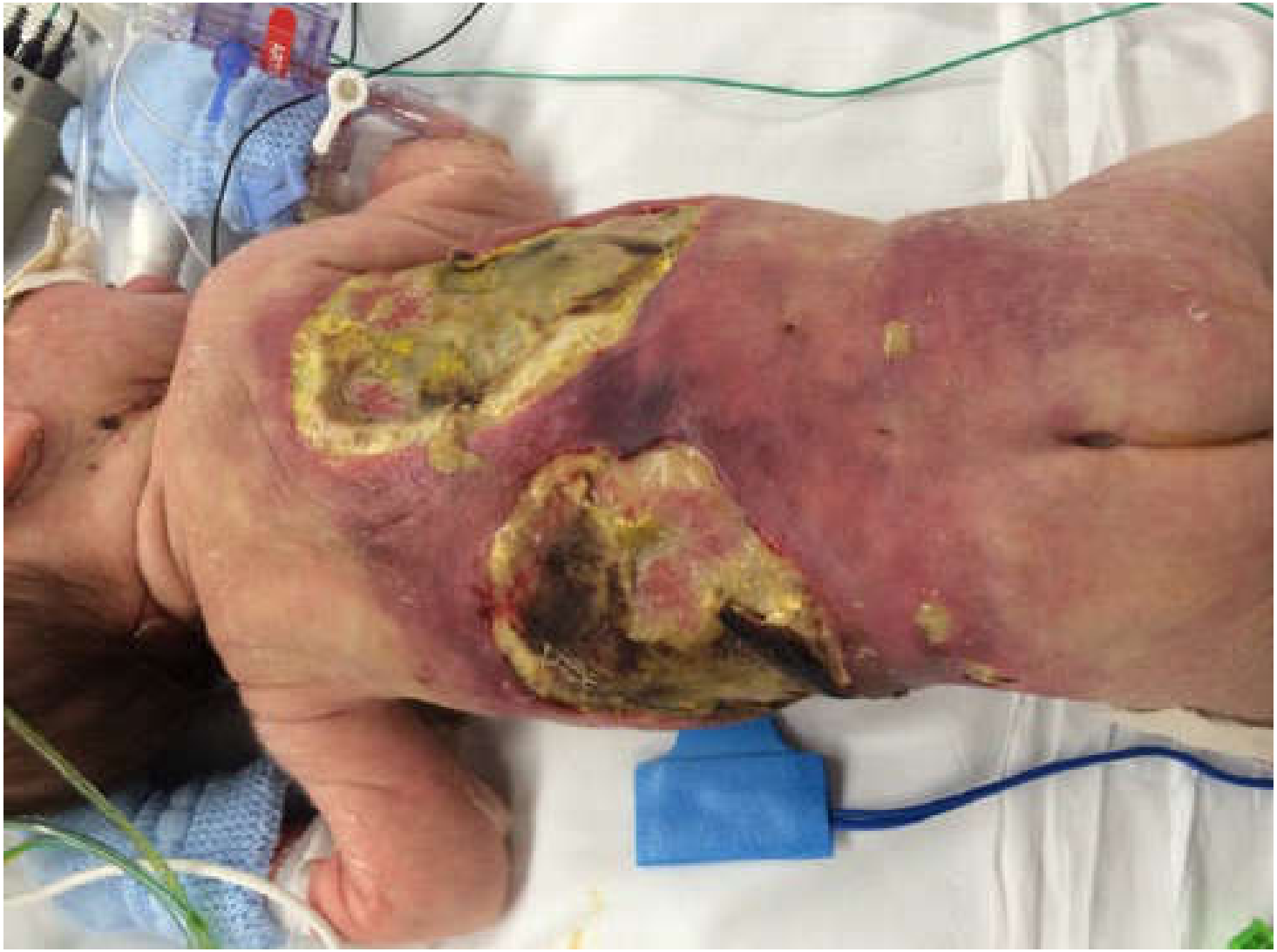


Neonatal Purpura Fulminans



Typical skin lesions of neonatal purpura fulminans

Neonatal Purpura Fulminans



Extensive full thickness necrosis of skin

Initial treatment

- Fresh Frozen Plasma
- Protein C concentrate

Fresh Frozen Plasma

- Class I, level A
- Administration of 10 – 20 mL/kg of FFP every 12 hours until the clinical lesions resolve.

(Antithrombotic Therapy in Neonates and Children. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Guidelines)

Protein C concentrate

- Class I, level A
- Administration of 20 – 60 units/kg of protein C concentrate every 6 – 8 hours until the clinical lesions resolve.

(Antithrombotic Therapy in Neonates and Children. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Guidelines)

Long-term management

- Oral anticoagulation therapy
- Low molecular weight heparin
- Protein C concentrate
- Liver transplantation

Low molecular weight heparin

- Class I, Level C
- Subcutaneous administration every 12 hours
- 1.7 mg/kg in term infants, 2 mg/kg in preterm infants
- Goal: [anti-aFX] = 0.5 – 1 IU/ml
- Prophylaxis: 0.8 - 1 mg/kg
- Goal: [anti-aFX] = 0.1 – 0.3 IU/ml

(Viviana Bacciedoni et al. Thrombosis in newborn infants, *Arch Argent Pediatr* 2016;114(2):159-166)

(Antithrombotic Therapy in Neonates and Children. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Guidelines)

Warfarin

- Class I, Level C
- 0.2 - 0.3 mg/kg/d
- Goal: INR 2.5 – 4.5

(Viviana Bacciedoni et al. Thrombosis in newborn infants, *Arch Argent Pediatr* 2016;114(2):159-166)

(Antithrombotic Therapy in Neonates and Children. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Guidelines)

Protein C replacement

- Class I, Level B
- 30 - 50 units/kg every 1 - 3 days
- Intravenous or subcutaneous

(V.E.Price et al. Seminar in Fetal and Neonatal Medicine, *Elsevier* 2011: 1-5)

(Antithrombotic Therapy in Neonates and Children. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Guidelines)

Protein C replacement

Continuous subcutaneous infusion of protein C concentrate using an insulin pump in a newborn with congenital protein C deficiency

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We describe the case of a newborn presenting with multicystic encephalomalacy, hydrocephalus and bilateral hemovitreous. An underlying coagulation disorder was suspected and laboratory tests revealed severe protein C deficiency. At 25 days of life, after the appearance of purpura fulminans, replacement therapy with intravenous protein C concentrate (Ceprotin; Baxter, Vienna, Austria) was started. Due to difficulties in getting peripheral venous access and to repeated loss of the venous access, continuous subcutaneous infusion of protein C was started with an insulin pump (VEO 754; Medtronic, Minneapolis, Minnesota, USA), normally adopted in patients with type 1 diabetes mellitus. Protein C values increased into the normal range and the resolution of the purpuric skin lesion was achieved. Chronic prophylaxis with low-molecular-weight heparin failed and, due to cutaneous and cerebral recrudescence, replacement therapy with the pump was started again. The insulin pump allowed us to reduce the number of injections per day and to deal with the difficulties in getting peripheral venous access, permitting medical and paramedical staff an easier management of the therapy. The dosing schedule could be easily adapted with the insulin pump and the continuous subcutaneous administration of small amounts of protein C concentrate prevented fluctuation in trough levels of protein C. This is the first reported case of a novel, successful use of an insulin pump in an extremely rare disease, to administer a drug different from insulin, which needs to be further analyzed, underlining the importance of a multidisciplinary team approach in order to provide effective and efficient care in high-complexity diseases.

Blood Coagulation and Fibrinolysis 2014, **25**:522–526

Keywords: insulin pump, newborn, protein C deficiency, purpura fulminans, thrombophilia

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Received 28 October 2013 **Revised** 17 December 2013
Accepted 20 December 2013

Liver transplantation

- Class I, Level C
- Definitive cure

(Antithrombotic Therapy in Neonates and Children. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Guidelines)

Long-term Follow-up of Homozygote Protein C Deficiency After Multimodal Therapy

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Summary: Homozygous protein C deficiency is an extremely rare condition presenting in the neonatal period with purpura fulminans, with very high rates of morbidity and mortality. Optimal treatment for this condition is highly complex, poorly understood, and often limited by cost and product supply. We report a child who presented 2 days after birth with purpura fulminans and severe prenatal eye damage, but no cerebral lesions. He was treated with novel multimodal therapy culminating in liver transplant at 3 years of age. The patient is now 12 years of age, well, with blindness as his only long-term deficit.

Key Words: homozygous protein C deficiency, multimodal therapy, long term follow up

(*J Pediatr Hematol Oncol* 2014;36:e452–e455)

was discharged home after 24 hours, with breast-feeding established. On his second day of life, the domiciliary midwife discovered that both feet were dark purple and cold to touch. He was alert, afebrile, slightly irritable, and had a petechial rash around parts of the face and neck. The symptoms were quickly progressive, with both feet becoming severely affected, lesions forming on the right buttocks, and discoloration of the scrotum apparent on arrival at hospital (Fig. 1). Apart from the skin lesions, the examination was unremarkable. All arteries and veins were patent with faint feet pulses and no venous or arterial thrombus found on Doppler ultrasound of the abdomen and lower limbs. Cranial ultrasound was normal. A clinical diagnosis of purpura fulminans secondary to homozygote protein C or S deficiency was made. He commenced intravenous gentamycin and penicillin to prevent potential sepsis, and received 20 mL/kg of fresh frozen plasma (FFP) over 2 hours every 12 hours. A continuous 10 U/kg/h heparin infusion was also given when FFP was not running. The baby's protein C activity levels were lower than the minimal detectable levels for the protein C assays and the mother and father's protein C activity levels were

Thrombolytic therapy

- Life-, organ-, limb-threatening condition
- Not enough evidence for use in Neonatal Purpura Fulminans

Recommendations and level of evidence for treatment of NPF

	Class I Benefit >>> Risk Should be performed	Class IIA Benefit >> Risk Reasonable to performe	Class IIB Benefit ≥ Risk May be considered	Class III Risk ≥ Becifit Not helpful May be harmful
Level A Multiple (3 – 5) population risk strada evaluated	**. FFP** **. Protein C concentrate**			
Level B Limited (2 -3) population risk strada evaluated	**. Protein C longterm**			
Level C Very limited (1 -2) population risk strada evaluated	**. LMWH** . Warfarin . Liver transplantation			

Thank for your attention!