Splenic Sequestration in Sickle Cell Disease

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NORTHERN CALIFORNIA
NETWORK OF CARE
FOR SICKLE CELL DISEASE

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Objectives

- Review definition of splenic sequestration
- Review the natural history of splenic sequestration in SCD
- Review management of acute sequestration
- Discuss educational approaches to teach families about splenic sequestration

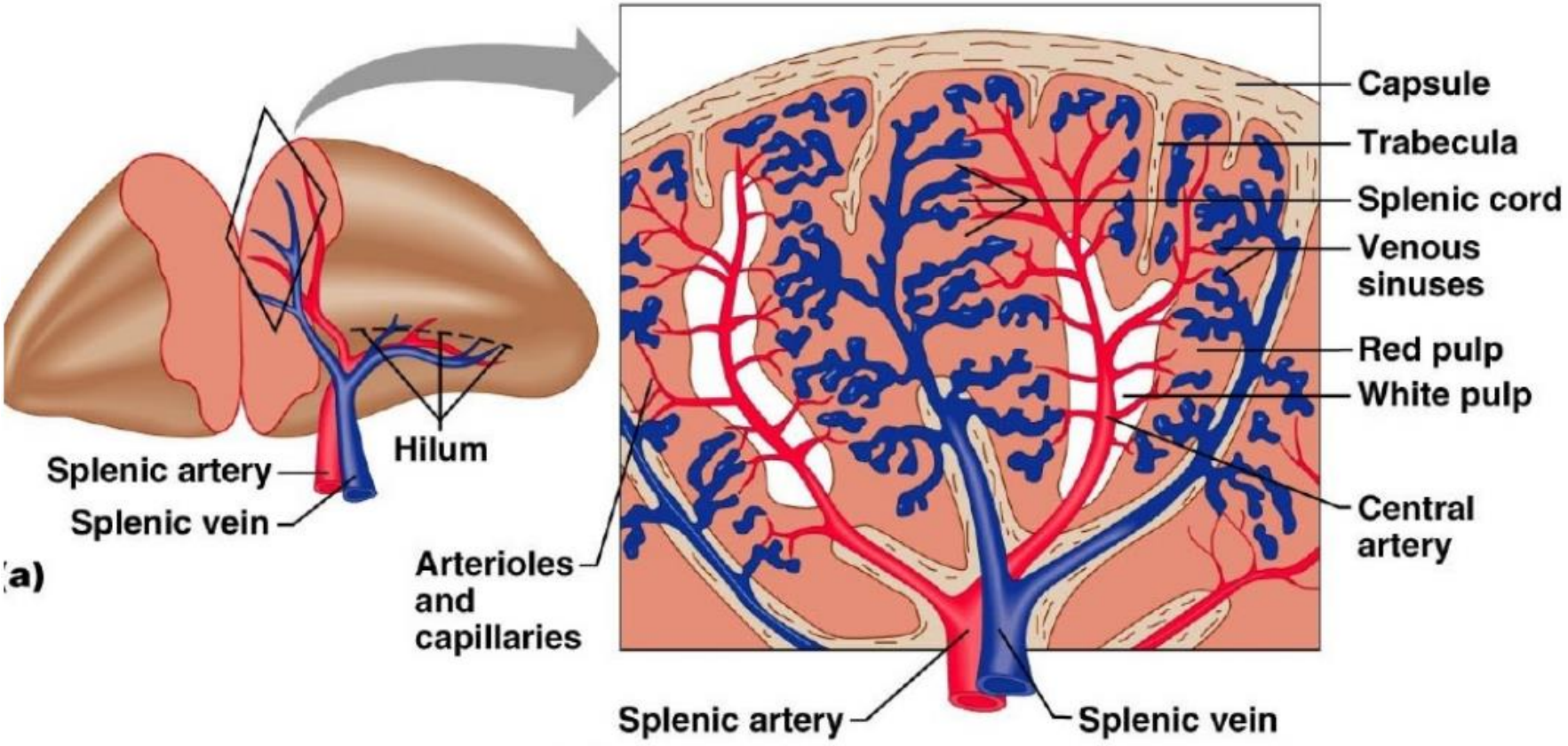
NHLBI Splenic Sequestration Recommendations

Evidence-Based Management of Sickle Cell Disease

Expert Panel Report, 2014

	Strength	Quality
1. In people with hypovolemia due to severe acute splenic sequestration, immediately provide IV fluid resuscitation.	Strong	Low
2. In consultation with a SCD expert, transfuse people who have acute splenic sequestration and severe anemia to raise the hemoglobin to a stable level, while avoiding over-transfusion	Strong	Low
3. In consultation with a SCD expert, address the performance & timing of splenectomy in people with recurrent acute splenic sequestration or symptomatic hypersplenism.	Moderate	Low

Spleen Anatomy



Pathophysiology of Sequestration

- Vaso-occlusion and pooling of RBCs within the spleen
  - Congestion of sickled RBCs in the red pulp
- Often see a concomitant sequestration of platelets
- May happen concurrent with illness
- May develop without warning and follow a fulminant and fatal course due to the development of hypovolemic shock

Spleen volume measurements, 7.5 – 18 months old

	N	Mean (SD)	Range
BABY HUG	199	105 (46)	28-281
Healthy controls	18	30 (14)	NA

MG McCarville. AJR 2011

Definition of Splenic Sequestration

- **Acute** drop in Hb (>2 g/dL) accompanied by:
  - Splenomegaly
  - Increase in reticulocytosis

- Acute can be hours, days, weeks

By the Numbers

- Kingston, Jamaica experience (natural history study)
- 1973 – 1981
- 308 kids followed (Hb SS only)
- 89 kids (29%) developed 132 episodes
- 13/132 episodes were fatal (9.8%)
- Cumulative probability of developing sequestration:
  - 22.5% by 2 yrs
  - 26.5% by 3 yrs
  - 29.7% by 5 yrs
- 49% experienced a recurrence

year, and every 3 months thereafter. They were encouraged to attend without appointment when sick, and an emergency service was provided outside of regular hours.

Of the 314 patients with SS recruited to the cohort study, six defaulted from follow-up at the beginning of the study, leaving 308 "at risk" for ASS. Of these, 14 children died from a cause other than ASS before their second birthday, and two others were later lost through default or migration, leaving a study group of 292 children. The survivors of this group were aged 2 years to 10 years 6 months at the time of analysis (December 31, 1983).

Routine hematologic procedures were used on both venous and capillary blood samples. Venipunctures were

AM Edmond. J Pediatrics 1985

By the Numbers

- Cooperative Study of Sickle Cell Disease (natural history study in USA)
- 1978 – 1988
- 694 kids followed (all genotypes)
- 43 kids (6%) developed 61 episodes of sequestration
- Median age at first event 1.6 yr*
- 2/43 patients had fatal episodes (4.6%)
- No episodes of post-splenectomy bacteremia

FM Gill. Blood 1995

*included only those who underwent splenectomy (n = 16)

Incidence in the CSSCD

- Hb SS vs Hb SC
- Incidence per 100 person-years by age

Age	SS	SC
<6 mo	1	0
6-12 mo	5.5	0
1	6.2	0.5
2	5.3	0
3	2	1.5
4	1.5	2.9
5	1.4	1.3
6	1	1.8
7	0	0
8-10	0	0

FM Gill. Blood 1995

Translating for Families

- Up to ~30% of pts will develop splenic sequestration
- Recurrence rate may be as high as ~50%
- Incidence is highest between the ages of 6 mo – 2 yrs
- Youngest reported case was in a 2 mo
- Can happen well into adulthood for those with variant sickle cell syndromes & those on hydroxyurea

A Pappo and GR Buchanan. Pediatrics 1989

Anticipatory Guidance

- Introduce topic of splenic sequestration early to families

Discussion time

How do you teach families to feel for the spleen?

How do you describe to them what it feels like?

Acute Management

- PRBC transfusion and IVF to restore intravascular volume
- Initiation of PRBC transfusion will often lead to release of sequestered blood by the spleen, a phenomenon known as “auto-transfusion”
- Be cautious not to over-transfuse, as this can lead to hyperviscosity-related complications
- Perform serial monitoring of Hb/Hct

Mgmt Beyond Acute Resuscitation

- Life-threatening episode → Splenectomy
- Recurrent episodes → Splenectomy
- Chronic splenomegaly with no acute episodes (yet) of splenic sequestration → Unclear

Total vs Partial Splenectomy?

- Little data to guide this decision
- TS is most common approach in clinical practice
- PS could potentially be considered for patients who are expected to have some residual splenic function, e.g.:
  - Hb SC
  - Hb S/beta + thalassemia
  - Residual function seen on liver-spleen scan

Open vs Laparoscopic?[1]

[1]T Goers. PBC 2008

Assessing Splenic Function

- Pitted RBC count
  - Pit count can be used to assess splenic reticuloendothelial function in patients with SCD
  - Pit count inversely related to splenic function
- Technetium-99m scan
- Howell-Jolly bodies
  - Nuclear remnants normally removed by the spleen
  - Their presence in peripheral RBCs indicates splenic dysfunction

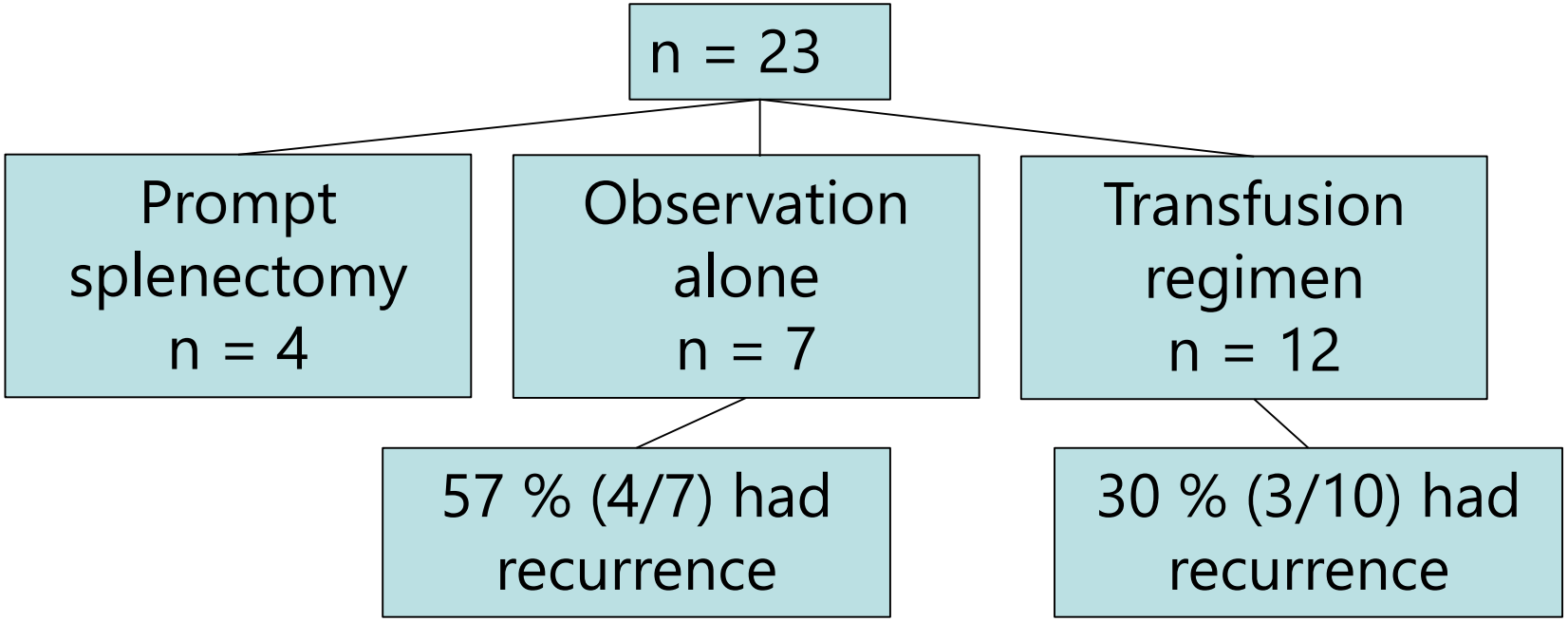
Does HU Protect the Spleen?

- BABY HUG Trial
- Hb SS or Hb S/β^0 thalassemia
- Ages 9 -18 months, n = 193
- HU 20 mg/kg/day vs placebo x 2 years
- Primary endpoint included splenic function, assessed by ^{99}Tc spleen scan (normal, decreased or absent)
- HU did not preserve splenic function
- Episodes of splenic sequestration were equal in both arms (12 events in both arms)

W Wang. Lancet 2011

Do transfusions protect against recurrence of splenic sequestration?

- Duke experience (retrospective)
- Median age 1.6 yr
- Mean drop in Hb 3.6 g/dL
- 75% also had thrombocytopenia (plt <150)



TR Kinney. J Pediatrics 1990

Do transfusions protect against recurrence of splenic sequestration?[1]

- Sequestration may occur despite reduction in Hb S concentration <30%
- Risk of recurrence was similar for pts who received transfusions versus observation
- Short-term transfusion program is of limited benefit

Do transfusions reverse functional asplenia?[2]

- One study suggests there may be at least partial restoration of function on chronic transfusions
- Risk likely outweighs potential benefit

[1]TR Kinney. J Pediatrics 1990
HA Pearson NEJM 1970

Post-Splenectomy Management

- Life-long penicillin?
- Aspirin?

Increased Pain Post-Splenectomy?

- Two studies suggest that there may be an increase in pain post-splenectomy
- Data is not strong, however

JG Wright. J Pediatrics 1999
A Piccin BJH 2009

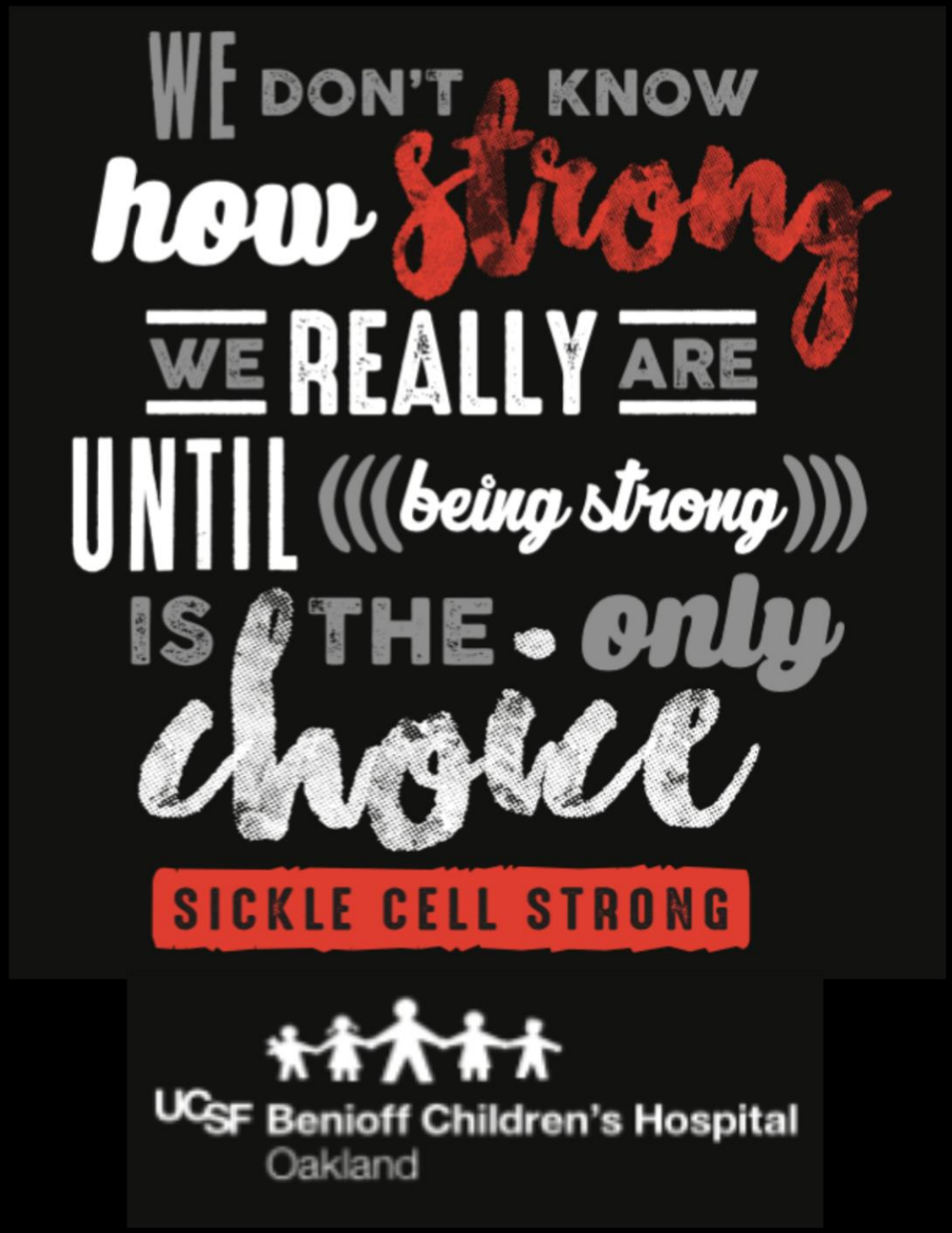
Does Splenectomy Increase risk of Death or Bacteremia?

- Kingston, Jamaica experience (retrospective)
- Median age 2.3 yr
- N = 130 underwent splenectomy over a 22 yr period
- Age & gender matched control group
- Examined death, bacteremia, pain, ACS
  - No difference in death (9 vs 12 in control arm)
  - No difference in bacteremia (10 vs 12 in control arm)
- No study, to date, in sickle cell demonstrates an increased risk of post-splenectomy sepsis/bacteremia

JG Wright. J Pediatrics 1999

Discussion

- Other specific sequestration cases people want to discuss?
- Questions/comments?


WE DON'T KNOW
how strong
WE REALLY ARE
UNTIL (((being strong)))
IS THE only
choice
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