Case 1: A Splitting Headache

- 42 y.o. African-American male presents with an acute-onset severe frontal headache while sitting on his front porch
- Past Medical History:
  - Sickle cell trait
  - Splenectomy for painful splenomegaly at age 32
  - Pulmonary embolism at ages 33 and 36, idiopathic, treated with 1 year anticoagulation each
- Meds: None
- Family history: Father with sickle cell trait, brother with MS, mother healthy.

Case 1

WHITE BLOOD CELL CNT	4500	11000	/cu mm		8790
RED BLOOD CELL COUNT	4.50	5.90	M/cu mm		5.03
HEMOGLOBIN	13.9	16.3	g/dL		12.2
HEMATOCRIT	41.0	53.0	%		37.1
MEAN CORPUSCULAR VOL	80.0	100.0	fL		73.8
MEAN CORPUSCULAR HGB	26.0	34.0	pg		24.3
MEAN CORPUS HGB CONC	31.0	37.0	g/dL		32.9
RBC DISTRIB. WIDTH	11.5	14.5	%		17.0
PLATELET COUNT	150	350	K/cu mm		241

- Admission MRI/A head: Sagittal vein thrombosis and bilateral transverse sinus thrombosis with associated frontal and cerebellar venous infarcts.

What would you do next?

A) Check iron studies given the anemia and microcytosis.

B) Perform a whole body CT to rule-out malignancy given the unusual clot location.

C) Perform a hemoglobin analysis to verify sickle cell trait.

D) No further work-up is required.

Answer

- C) Perform a hemoglobin analysis

Results: **Hemoglobin S 68.3%**, hemoglobin A 22.2 %, hemoglobin F 3.1%

SICKLE CELL DISEASE

(Sβ+ thalassemia)

Case 1

- Prot C activity/antigen -94%/84%
- Resistance to activated prot C- 2.6
- Alpha-2 antiplasmin -106%
- Homocysteine- 7.9
- Fibrinogen – 307
- ATIII- 86%
- Prot S activity/antigen 61%/115
- Prothrombin mutation – normal
- RVVT confirm- 1.4
- Cardiolipin abs negative

CARDIOLIPIN IGG AB			GPL Units	6 *
CARDIOLIPIN IGM AB			MPL Units	9 *
CARDIOLIPIN IGA AB			APL Units	3 *
BETA-2 GLYCOPROT. IGG	0	20	STD IgG un	2
BETA-2 GLYCOPROT. IGM	0	20	STD IgM un	3
BETA-2 GLYCOPROT. IGA	0	20	STD IgA un	11

Case 2

- 28 yr old with SCA presents to the ED with two days of chest pain. Reports pain started while she was at work. She denies any SOB. She denies any lower extremity swelling.
- Reports pain is similar to her prior VOC pain, she has pain on inspiration. She has a history of multiple episodes of acute chest syndrome.
- Vitals: T 97.5, P74, BP 97/72, 99% on 2L GEN: slightly uncomfortable but otherwise well appearing CV: RRR, normal S1/S2, no m/g/r LUNGS: Clear without wheezes or crackles ABD: soft, nt, nd, +bs EXT: warm and dry. no c/c/e.

Case 2

- Pain is treated in ED and CXR is negative
- Pt is discharged home
- Returns two days later to sickle clinic reporting pain is not improved.
- CT with contrast of the chest reveals pulmonary emboli in the distal left upper lobar artery, left lingular segmental, and bilateral lower lobe segmental arteries.

Case Question

How would you manage this patient's anticoagulation (AC)?

A) Initiate AC immediately and continue indefinitely for idiopathic PE.

B) Initiate AC immediately and continue short-term AC for a hospital-triggered PE.

C) No AC is warranted because this is likely an *in situ* thrombosis.

D) Check d-dimer, APLS-antibodies, and protein C/S levels and initiate AC if abnormal.

Case 2

A) Initiate AC immediately and continue indefinitely for idiopathic PE.

Key points

- Sickle hypercoaguable state and must think about diagnosis even if case is atypical.
- Classic pleuritic chest pain attributed to a vaso-occlusive crisis
- Likely limit work-up to antiphospholipid work-up.
- Remember d-dimer often elevated at baseline so not a helpful diagnostic tool.
- Would strongly consider indefinite anticoagulation.

Case 3

- 25 yr old AA woman with sickle cell anemia comes for routine visit to your clinic
- Complications:
  - Stroke at the age of 5 and had been on chronic transfusion therapy but decided to stop that at the age of 18.
  - Acute chest syndrome 5 yrs prior.
- Medications include hydroxyurea and oxycodone as needed for pain.
- She has not been hospitalized in over a year and reports that she is doing well.
- She has a new boyfriend and asks you what she should do for birth control.

Question Case 3

You recommend:

A) As she has a history of a stroke you recommend that she not take oral contraceptives as the risk of these agents are higher than that associated with pregnancy in SCD.

B) She can take any oral contraceptive currently available as there has not been any increased risk associated with their use in SCD

C) You recommend a progestin only contraceptive as there is data that it might decrease her vaso- occlusive crisis frequency and the risks of taking these are less than the risks associated with pregnancy.

Case 3

- C) You recommend a progestin only contraceptive as there is data that it might decrease her vaso-occlusive crisis frequency and the risks of taking these are less than the risks associated with pregnancy.
- A history of stroke is a contraindication to combined hormonal contraception, and by age 20, approximately 11 percent of untreated women with SCD have had a clinically apparent stroke
- Two controlled clinical studies- found a decrease in VOC with the use of Depo-Provera (DMPA).·
  - This non-contraceptive benefit led ACOG to suggest DMPA as a recommended contraception for women with SCD.
  - Unclear if the decrease in pain crises is secondary to amenorrhea, or secondary to the effect of progesterone on the sickling process and other hematological parameters..

Contraception 1997;56:313-6.
The Lancet 1982;2:229-31.
Obstetrics and Gynecology 2006;107:1453-72.
Journal of Obstetrics and Gyn 2002;22(4):399-401.

Pregnancy Complications

17,952 deliveries c/w controls using national inpatient database from 2000-2003

Diagnosis	OR	95% CI	p value
Thrombotic complications			
Deep vein thrombosis	2.5	1.5-4.1	<0.001
Cerebral vein thrombosis	4.9	2.2-10.9	<0.001
Infectious complications			
UTI	2.3	1.9-2.7	<0.001
Pyelonephritis	1.3	1.0-1.8	0.05
Pneumonia	9.8	8.0-12.0	<0.001
SIRS	12.6	2.1-13.6	0.01
Sepsis	6.8	4.4-10.5	<0.001
Postpartum infection	1.4	1.1-1.7	<0.001

Adapted from Villers et al. *Am J Obstet Gynecol* 2008.

Pregnancy Complications

Diagnosis	OR	95% CI	p value
Fetal Complications			
IUGR	2.2	1.8-2.6	<0.001
Preterm labor	1.4	1.3-1.6	<0.001
Obstetric complications			
Gestational HTN & preeclampsia	1.2	1.1-1.3	0.01
Eclampsia	3.2	1.8-6.0	<0.001
Antepartum bleeding	1.7	1.2-2.2	<0.001
Postpartum hemorrhage	0.5	0.3-0.6	<0.001
Abruption	1.6	1.2-2.1	<0.001

Mortality rate for women with SCD:
72.4 deaths/100,000 deliveries v. 12.7/100,000 deliveries for women w/o SCD.

Case 4

- 11 year old girl with sickle cell anemia presents with cough, fever, and abdominal discomfort as well as a mild headache. On admission, her hgb is 2.7 g/dL and reticulocyte count is 0.1%. PCR detects parvovirus B19.
- She received transfusions to Hgb of 10 g/dL. Three days later she developed severe bilateral frontal headache with photophobia and phonophobia.
- MRI shows area of restricted diffusion in R. superior frontal lobe consistent with acute stroke.
- Transthroracic echocardiography shows a patent foramen ovale.

Question

What would you do next?

A) Start patient on chronic transfusion therapy and no further work-up is needed

B) Start chronic transfusion therapy and check for acquired hypercoaguable states?

C) Start anticoagulation and no further work-up is needed

Answer

- B) Start chronic transfusion therapy and check for acquired hypercoaguable states?

Case 4 continued

- Lab studies show dRVVT of 68.4 with confirm ratio of 1.9, APL antibodies with ACL IgM and IgG and beta 2 glycoprotein IgM and IgA. Factor VIII activity is elevated at 185%.
- Both sickle cell anemia and parvovirus B19 infection can predispose to the generation of antiphospholipid antibodies.
- Patient anticoagulated and started on chronic transfusion therapy.
- APL titers returned to normal and warfarin was discontinued at 18 months. At 4 years follow-up, patient has had no recurrent episodes.