

Antiphospholipid syndrome (APS)& pregnancy

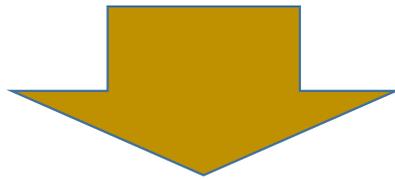
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Antiphospholipid syndrome (APS)

- autoimmune disorder
- venous or arterial thrombosis
- and/or
- pregnancy loss in the presence of **persistent** antiphospholipid antibodies (aPL).
- lupus anticoagulant (LA),
- anticardiolipin antibodies (aCL),
- anti-beta-2-glycoprotein-1 antibodies.
- **Of note, aPL can also be found in healthy individuals.**

Treatment of APS during pregnancy

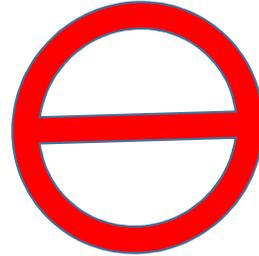


- **reduces** the frequency of **thrombosis**
- **reduces** the risk of an **adverse pregnancy outcome**

Sapporo (or Sydney) criteria

- defining pregnancy morbidity in the diagnosis of APS
- **≥1 unexplained fetal deaths ≥10 w** with normal anatomy
- **≥1 preterm deliveries of a normal infant before 34 due to preeclampsia, or placental insufficiency**
- **placental insufficiency include :**
 - •Abnormal or nonreassuring fetal surveillance tests (eg, lack of fetal heart rate acc. low score on BPP)
 - •Abnormal Doppler
 - •Oligohydramnios
 - •Birth weight <10th percentile
- **•≥3 unexplained, consecutive, spontaneous pregnancy losses <10 w** after exclusion of maternal anatomic and hormonal abnormalities and paternal and maternal chromosomal abnormalities.

placental abruption



- Although placental abruption has been associated with placental insufficiency,
- APS is not associated with abruption,
- placental abruption is not a defining morbidity for APS.

higher risk of adverse outcome

LA major predictor

39 % of patients with LA poor

13 % for IgM anti-beta-2-glycoprotein-1.

"Triple positivity" only 30 percent had a live birth with tx ASA & CELEXAN

8 % for (IgG) aCL,

0 % for IgM aCL,

0 % for IgG anti-beta-2-glycoprotein-1,

mechanism for adverse pregnancy
outcome

Uteroplacental thrombosis

vascular insufficiency may be one

hallmark of APS

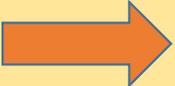
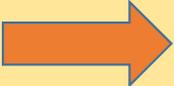
Thromboses are the hallmark of APS,

venous thromboses are more common than arterial.

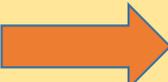
The **deep veins of the lower extremities** are the most common sites of venous thrombosis

the cerebral vasculature (stroke and transient ischemic attack) is the most common site for arterial thrombosis.

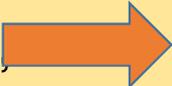
risk of thromboembolic disease

- during pregnancy or postpartum
- among APS  5 to 12 percent ,
- the general obstetric population  0.025 to 0.10 percent

Anticoagulation

- . *prefer LMWH to UFH*
- *avoid oral anticoagulants,*  *warfarin*
- *factor Xa inhibitors*  *fondaparinux*
- ***Direct oral anticoagulants:***
 - rivaroxaban, dabigatran* may be *ineffective* in APS
 - *should not be used*
 - *they cross the placenta*
 - *lack of safety data*

(prophylactic versus therapeutic)

- depends on the indication for anticoagulation,
- If heparin **is contraindicated** because of heparin-induced thrombocytopenia (HIT)  danaparoid or fondaparinux are reasonable options

The optimum low dose of aspirin (ASA),

- , is unclear.
- optimum dose to **reduce the risk of preeclampsia** may be 100 to 150 mg,
- 81 mg is a **more practical dose** as 100 to 150 mg
- Taking one and one-half 81 mg tablets is an option.

Selection of patients for antithrombotic therapy

varies depending on

whether they have APS based on a
prior thrombosis versus

an APS-associated **pregnancy**
morbidity

APS based on aPL and **prior thrombosis**, with/without APS-defining pregnancy morbidity

- lab. criteria for aPL
- history of arterial or venous thrombosis
 - **high risk of recurrent thrombosis**
- treated with warfarin for an indefinite period that may be lifelong

***...APS based on aPL and **prior thrombosis**, with/without
APS-defining pregnancy morbidity***

- American College of Chest Physicians (ACCP)



- **use of LMWH anticoagulation**

- Risk of thrombosis



-
-
-

in untreated patients 10 %

in treated patients, less than 1%

prior thrombosis

We prefer

LMWH

greater safety
and efficacy
compared
with UFH,

but UFH is an
acceptable
alternative.

APS based on aPL **and prior thrombosis**, with/without APS-
defining pregnancy morbidity

**therapeutic dose
of LMWH**, as
suggested by the
American College of
Rheumatology (ACR)



low-dose ASA,
reduce **the risk**
criteria for
preclampsia

Aspirin reduce
the risk of
arterial
thrombosis.

APS based on aPL and APS-defining pregnancy morbidity alone, **no prior thrombosis**

We offer **pharmacologic treatment**

experts consider **close clinical surveillance**

with or without the addition of **hydroxychloroquine** to be a reasonable alternative approach

Early or late loss

combined
therapy with

low-dose ASA
beginning
when
**conception is
attempted,**



prophylactic-
dose LMWH
upon
**confirmation
of intrauterine
pregnancy;**

improvement
in outcome
with combined
therapy.

Preterm delivery related to uteroplacental insufficiency

Low-dose ASA therapy

beginning at the **end of the first trimester** and continuing through delivery

some clinicians prescribe LMWH, available evidence **does not support this approach**

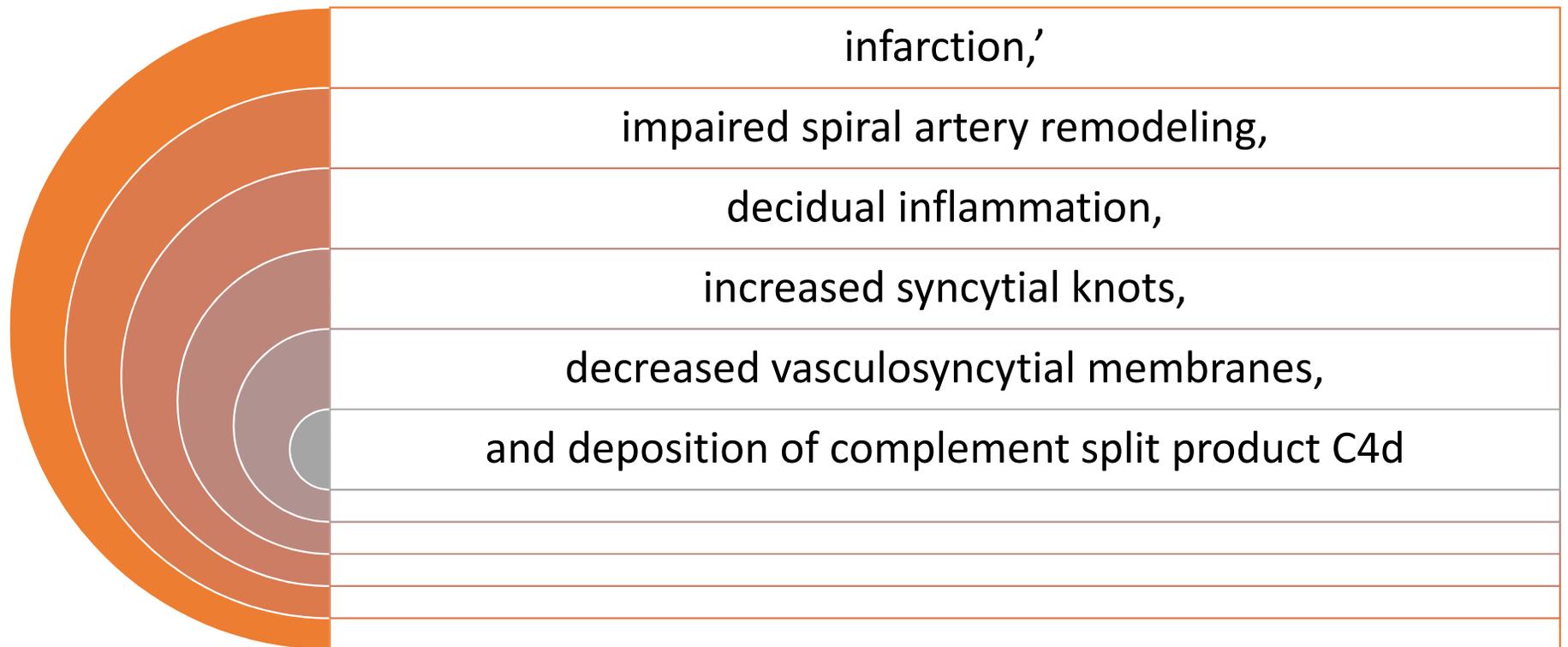
cases of ASA failure

in cases of ASA failure

or when placental examination shows extensive decidual inflammation and vasculopathy and/or thrombosis

prophylactic-dose LMWH with low-dose ASA selectively

common histopathologic features of the placenta



Antepartum maternal and fetal monitoring

intervention in the event of maternal or pregnancy complications, such as preeclampsia.

Baseline platelet count, creatinine, urine protein-to-creatinine ratio, (ALT), (AST) for comparison in the event of active APS or other complications later in pregnancy.

anti-Ro/SSA and anti-La/SSB antibodies

serial sonograms approximately **every four weeks** beginning in the late second or early third trimester

fetal well-being (nonstress tests and/or BPP)

because of the increased risk of antepartum fetal death

beginning at 32 weeks

Weekly

or twice per week

Labor and delivery

In the absence of standard medical or obstetric indications for early delivery,



TO control the timing of **discontinuation** of antithrombotic drugs

schedule delivery (induction or cesarean) **at 39 weeks**

Anticoagulation

therapeutic LMWH **switch to** therapeutic doses of UFH at 36 to 37 week

24-h interval between therapeutic LMWH and placement of an **epidural catheter**

(at least **12 h** for prophylactic dose).

Therapeutic UFH DC 24 h before labor and delivery,

patients with prior thromboses are not off anticoagulants **for more than 48 hours**

Low-dose ASA

stopped after 36 weeks in women **with no history of thrombosis.**

Stopping ASA 7 to 10 days before delivery minor perioperative bleeding

past history of **serious arterial thrombotic complications**, such as stroke or myocardial infarction, we **continue ASA through labor and delivery**

Postpartum care

— APS by lab. criteria and a prior history of **arterial or venous thrombosis**

high risk of recurrence

4 to 6 hours after NVD or 6 to 12 hours after CS,

indefinite period of anticoagulation with warfarin

Postpartum care

APS based only on obstetric morbidity (no venous or arterial thrombotic events)

who have an early pregnancy loss

not administer anticoagulation after expulsion of the products of conception.

**PATIENTS WITH POOR PREGNANCY OUTCOME DESPITE
ANTITHROMBOTIC THERAPY**

no second line therapy with proven efficacy.

hydroxychloroquine appears to depress aPL levels

***might be beneficial in women with APS-related recurrent
pregnancy loss***

**three months for HQ to have an effect, thus it should be started
prior to pregnancy.**

Pregnancy outcomes of women **with aPL** without APS

— It is unclear whether women with aPL who do not meet criteria for APS are

increased risk of pregnancy morbidity.???

risk of first-time thrombosis in pregnant women with aPL and no personal history of thrombosis ???

aPL and primary infertility,???

(IVF) failure???

near-term/term preeclampsia???

measurement of aPL during pregnancy is **unnecessary**

Most patients without APS who are aPL positive in the first trimester (defined as aCL or anti-beta-2-glycoprotein-1 ≥ 40 units or LA-positive) **remain in the high-positive range throughout pregnancy**

Modest decreases in aPL observed during pregnancy but **not changes in pregnancy outcomes.**

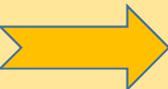
Conversion from **negative to positive antibody** tests occurs infrequently and is not associated with adverse pregnancy outcomes.

repeat measurement of aPL during pregnancy is **unnecessary.**

aPL⁺ without APS

- Although associations between aPL and pregnancy morbidity have been reported in women without APS,
- **the association is weak**

management of pregnant women with the **incidental finding** of persistent aPL 

- **Over 50 percent**  **successful pregnancy without drug treatment**



Therapeutic options in pregnancy APL

no therapy,

low-dose aspirin (ASA; 50 to 150 mg per day) alone,

or low-dose ASA and prophylactic-dose heparin

treatment decisions should be made on an **individual basis**

avored prescribing low-dose ASA alone during pregnancy

????????????????

IVF in women with aPL⁺

- **not prescribe prophylactic antithrombotic** during IVF for women **with aPL & no clinical criteria for APS**
- not appear to adversely affect pregnancy rates or outcome
- (ASRM) concluded that **assessment of aPL** was **not indicated among** couples undergoing IVF ???
- American Society for Reproductive Immunology Antiphospholipid Antibody Committee **assessment of aPL indicated** among couples undergoing IVF ???

IVF in women with APS⁺

IVF is potentially dangerous since ovulation induction regimens trigger an **estrogen-induced hypercoagulable state**

high R. for women with a prior venous thromboembolism and APS.

If performed, women with a history of thrombosis-associated APS should be **switched from their usual oral anticoagulant to therapeutic dose UFH, which should be maintained after oocyte retrieval**

All complications occurred in cycles that included

(GnRH) agonists for ovulation induction.

Using a GnRH antagonist protocol or natural cycles **may minimize risk of thrombosis.**

Neonatal APS

aPL in the neonate almost always results from placental transfer of maternal antibody

thus may not have the same significance as endogenously produced antibody.

Passively acquired aPL completely disappears **by 6 to 12 months of age**

pregnant and postpartum women with APS or aPL

	Antepartum	Postpartum
APS with prior arterial or venous thrombosis, with or without APS-defining pregnancy morbidity	Therapeutic -dose LMWH and low-dose ASA	Warfarin for an indefinite period of time.

Antepartum	Postpartum
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APS based on laboratory criteria for **Apl+** and **APS+-** defining pregnancy morbidity of ≥ 1 fetal losses ≥ 10 weeks of gestation or ≥ 3 unexplained consecutive spontaneous pregnancy losses < 10 weeks of gestation and **NO history of arterial or venous thrombosis**

Prophylactic-dose LMWH and low-dose ASA

Prophylactic-dose **LMWH** and **low-dose ASA for six weeks**, regardless of route of delivery

Antepartum

Postpartum

APS based on laboratory criteria **for aPL+ and APS+** defining pregnancy morbidity of ≥ 1 preterm deliveries + of a morphologically normal infant before 34 weeks of gestation due to severe preeclampsia, eclampsia, or other findings consistent with placental insufficiency and NO history of arterial or venous thrombosis

Most cases: Low-dose ASA

Vaginal delivery: Intermittent pneumatic compression and low-dose ASA while in the hospital. Graduated compression stockings and **low-dose ASA for six weeks.**
Cesarean delivery: Prophylactic-dose LMWH and low-dose ASA for **six weeks**

Antepartum	Postpartum
<p>In cases of ASA failure or when placental examination shows extensive decidual inflammation and vasculopathy and/or thrombosis, prophylactic-dose LMWH with low-dose ASA</p>	<p>Prophylactic-dose LMWH and low-dose ASA for six weeks regardless of route of delivery</p>

	Antepartum	Postpartum
<p><i>APL+ but NO clinical criteria for APS (ie, NO thrombosis and NO history of APS-defining obstetric morbidity)</i></p>	<p>Low-dose ASA</p>	<p><i>Vaginal delivery:</i> <i>Intermittent pneumatic compression and low-dose ASA while in the hospital. Graduated compression stockings and low-dose ASA for six weeks.</i></p> <p><i>Cesarean delivery:</i> <i>Prophylactic-dose LMWH and low-dose ASA for six weeks.</i></p>

