Antiphospholipid Syndrome

APS · Thrombosis or pregnancy morbidity plus persistent antibodies — and warfarin, not a DOAC

NO DOACs
in triple-positive APS

DIAGNOSE IT *a clinical event plus a persistently positive antibody — both are required*

THE CLINICAL EVENT

Vascular thrombosis — venous, arterial, or small vessel, in any territory. Or **pregnancy morbidity**: recurrent early miscarriage, fetal loss after 10 weeks, or **premature delivery for severe pre-eclampsia or placental insufficiency**.

THE ANTIBODIES

Lupus anticoagulant · **anticardiolipin** IgG or IgM · **anti-β2-glycoprotein I** IgG or IgM. Must be at **medium or high titre** and, critically, **persistently positive on repeat testing at least 12 weeks apart** — transient positivity is common after infection.

TRIPLE POSITIVITY

All three antibodies positive marks the **highest-risk phenotype**, with the greatest recurrence risk. **It also defines the group in whom DOACs are unsafe**, so establishing the antibody profile is not academic.

ANTICOAGULATE CORRECTLY *this is where the harm happens*

Situation	Approach
Venous thrombosis	**Warfarin, target INR 2.0–3.0**, generally **indefinitely** given the high recurrence rate after an unprovoked event in APS.
Arterial thrombosis	**Warfarin**, with some authorities targeting a **higher INR (3.0–4.0)** or adding **low-dose aspirin**. Arterial events carry a worse prognosis and a lower threshold for intensified therapy.
DOACs	**Warfarin remains the first-choice agent.** The **TRAPS** trial randomized high-risk **triple-positive** patients to rivaroxaban or warfarin and was **stopped early**: **12% had arterial thrombotic events on rivaroxaban versus 0% on warfarin**, with roughly half occurring in the first 4 months. Two-year follow-up showed events in **33% who remained on a DOAC versus 6% on warfarin**.
Already on a DOAC?	If the patient is triple-positive or has had an arterial event, **switch them to warfarin**. Guidance permits considering DOACs only in **selected non-triple-positive** patients under specific circumstances, and several bodies recommend against them in APS altogether.

PREGNANCY *a treatable cause of recurrent loss — and the reason to test*

1. **Obstetric APS without prior thrombosis: low-dose aspirin plus prophylactic low-molecular-weight heparin** through pregnancy, continued for **6 weeks postpartum**, when the thrombotic risk is highest.
2. **Thrombotic APS in pregnancy: switch warfarin to therapeutic LMWH** as soon as pregnancy is confirmed — **warfarin is teratogenic**, with a defined embryopathy in the first trimester. Plan this **before** conception, not after a positive test.
3. **Hydroxychloroquine** is increasingly used as an adjunct, particularly with coexisting lupus, and appears to reduce thrombotic risk.
4. **Screen for APS in the right patients** — unprovoked thrombosis in the young, thrombosis at unusual sites, recurrent miscarriage, arterial events without atherosclerotic risk factors, and anyone with lupus.

CATASTROPHIC APS & OTHER TRAPS *the rare presentation that kills, and the lab pitfalls*

CATASTROPHIC APS

Multi-organ thrombosis over days with histological small-vessel occlusion — kidney, lung, brain, heart, skin. Mortality is high. Precipitated by **infection, surgery, or anticoagulation withdrawal**. Treat with **anticoagulation, high-dose glucocorticoids, and plasma exchange and/or IVIG**, plus **rituximab or eculizumab** in refractory cases — and treat the trigger.

LABORATORY PITFALLS

Lupus anticoagulant testing is unreliable while on anticoagulation — heparin, warfarin and DOACs all interfere, so interpret with the hematology laboratory. **A prolonged aPTT that does not correct on mixing** suggests a lupus anticoagulant. **The name is a misnomer**: it prolongs a test tube clotting time but causes **thrombosis**, not bleeding. Also expect a **false-positive syphilis serology** and mild thrombocytopenia.

WHO TO TEST, AND WHAT ELSE APS DOES *beyond the classic clot*

Prompt to test	Detail
Unprovoked thrombosis in the young	Venous or arterial thrombosis under about 50 without conventional risk factors, or thrombosis at an **unusual site** — cerebral venous sinus, hepatic, portal, mesenteric.
Recurrent pregnancy loss	Three or more early losses, any loss after 10 weeks, or delivery before 34 weeks for severe pre-eclampsia or placental insufficiency.
Autoimmune disease	**Screen everyone with lupus** at diagnosis. Also test with an unexplained prolonged aPTT, unexplained thrombocytopenia, or livedo reticularis.
Non-criteria features	Recognize them even though they do not classify the disease: **thrombocytopenia, livedo reticularis, cardiac valve disease** (Libman-Sacks vegetations), **APS nephropathy**, cognitive dysfunction, and chorea.

MANAGING RISK BEYOND ANTICOAGULATION *the parts that are routinely forgotten*

REDUCE THE OTHER RISK FACTORS

Stop smoking and avoid **estrogen-containing contraception and hormone replacement**, both of which compound thrombotic risk substantially. Treat hypertension and lipids. Give **thromboprophylaxis at high-risk times** — surgery, immobility, hospital admission — even in antibody-positive patients who have never clotted.

ASYMPTOMATIC ANTIBODY CARRIERS

Persistently positive antibodies **without** thrombosis or pregnancy morbidity is **not** APS and generally does **not** warrant full anticoagulation. **Low-dose aspirin may be considered** in high-risk profiles such as triple positivity or coexisting lupus, alongside aggressive risk-factor control and prophylaxis at high-risk moments.

PEARLS & PITFALLS

- **Do not use a DOAC in triple-positive APS.** TRAPS showed a 12% arterial event rate versus 0% on warfarin and was stopped early for harm.
- **One positive antibody is not APS.** Confirm persistence at 12 weeks — transient positivity after infection is common and over-diagnosis commits people to lifelong anticoagulation.
- **Lupus anticoagulant causes clotting, not bleeding**, despite the prolonged aPTT.
- **Warfarin is teratogenic** — plan the switch to LMWH before conception in any woman of childbearing age.
- **Continue anticoagulation postpartum for 6 weeks**, the period of highest thrombotic risk.
- **Stopping anticoagulation can precipitate catastrophic APS.** Interrupt it deliberately and briefly, with a plan, not casually for a minor procedure.

References: TRAPS trial of rivaroxaban in antiphospholipid syndrome and its two-year follow-up · EULAR recommendations for the management of antiphospholipid syndrome in adults · meta-analysis of DOACs versus vitamin K antagonists in APS (JACC, 2022).

Educational aid; verify doses against local hematology protocol and patient factors.