One-Page Summary: Antiphospholipid Syndrome. Dr. Sarah Goglin

Pathogenesis: Hemostatic reactions (pro-coagulant and anti-fibrinolytic); Activated cellular elements (endothelial cells, monocytes and platelets); Complement activation (activation of endothelial cells, proinflammatory environment, induction of thrombosis)

+aPL carriers and risk for thrombosis: 2.3% per patient year, 15-year cumulative risk approx. 30%. Persistent aPL were significantly a/w increased risk of 1st thrombosis, triple aPL positivity increased by three-fold the risk of 1st thrombosis
Stratify based on 1) aPL type and titer (high risk: LA pos, triple positive; mod risk (+aCL at med/high titers; low risk: isolated aCL or antib2GPI at low/med titers), 2) persistence of aPL profile; 3) presence of other prothrombotic risk factors
APLASA: RCT of 1o prevention of thrombosis in asymptomatic aPL+ subjects (+LA and/or aCL>=20-not necessarily high titers). No difference in risk of 1st thrombosis in ASA vs placebo at approx. 2.5 years. Event rate was low, low-risk group. Meta-analysis adjusting for CVD risk factors: 2-fold reduction in risk of 1st thrombotic event in tx group (with ASA).
1o prevention in pts without SLE: No prospective data support for empiric tx with ASA. No data for HCQ (RCT terminated early). Recommendation: LDA in aPL+ pts with high risk profile and/or presence of other thrombotic risk factors. Modify prothrombotic risk factors
1o prevention in pts with SLE: Consider LDA and HCQ (from observational studies suggesting protective effect) in mod/high aPL+ SLE pts. Modify prothrombotic risk factors.

Treatment of thrombotic APS (2o prevention): Rheum: favors high dose warfarin (retrospective studies, however); Heme: RCT shows no difference in standard vs high dose warfarin (however, short follow up, pt with recurrent events excluded, fewer arterial events, pts on high intensity tx were only 40% in target of INR 3-4).
Venous thrombosis: UFH or LMWH followed by warfarin (target INR 2-3). Arterial thromboses: Similar with venous. Goal INR of 3-4 preferred by some. ASA monotherapy may be sufficient in older adults with stroke and low titer aCL.

APS and pregnancy: D/c warfarin due to teratogenicity prior to pregnancy or immediately upon becoming pregnant; start on another form of AC. In obstetric APS: combo heparin and ASA is superior to ASA alone in enhancing live birth (also reduces risk of preeclampsia). If obstetric APS: prophylactic dose of UFH or LMWH plus ASA. Continue for approx. 6 weeks postpartum. If thrombotic APS: full dose LMWH or UFH and LDA. Transition to warfarin after delivery. UFH, LMWH and warfarin are compatible with breastfeeding.

APS and DOACs: Prefer warfarin over DOACs (rivaroxaban is not non-inferior to VKA; more strokes and potentially increased risk for recurrent thrombosis in certain groups of pts on rivaroxaban).

CAPS (1% of pts with APS): Precipitating factors: infection, surgery among the most common. If SLE, CYC may have a role. Tx: Heparin, pulse steroids, +/-Plasma exchange, +/-IVIG, +/-RTX. In refractory cases: eculizumab

Q+A pearls:
How frequently do you check aPL: at diagnosis of SLE; then recheck only when clinically relevant (for example when considering contraceptives or pregnancy)
“Seronegative” APS: May check extended panel of aPLs
IgA role: Specificity is lower compared to IgG/M. If clinical scenario with thromboses and only positive IgA, would consider as APS.
Recurrent thromboses while on warfarin: Has INR been in therapeutic range? Can consider increasing to high intensity; may add HCQ. Not usually adding ASA as increased risk for bleeding. Or may switch to LMWH.