# ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome - APS

- clinical condition associated with often multiple venous and arterial thromboses and recurrent fetal loss
- frequently accompanied with thrombocytopenia and neurologic signs,...
- consequence of prothrombotic action of antiphospholipid antibodies (LAC and aCL)

Prothrombotic action of antiphospholipid antibodies

consequence of the action on:

- cellular components (platelets)
- humoral components (natural anticoagulants)

Antiphospholipid syndrome
- clinical associations

- vascular – thrombosis, mb Buerger, atherosclerosis,
- cardial - myocardial infarction, valve disease, cardiomyopathy
- haematological – thrombocytopenia, AIHA
- CNS – migraine, chorea, CVA/TIA, psychosis, epilepsy
- skin – livedo reticularis, ulcers, superficial TF,...
- bone - avascular necrosis, bone marrow necrosis
- renal – renal a/v thrombosis, glomerular thrombosis
- pulmonary – embolism, hypertension, ARDS
- gastrointestinal – hepatic necrosis, Budd-Chiari,...
- endocrine – adrenal failure, hypopituitarism
- obstetric – recurrent miscarrriage, preeclampsia, growth retardation, HELLP

Main features of the APS

Clinical

- venous thrombosis
- arterial thrombosis
- thrombocytopenia

Laboratory

- IgG aCL (moderate/high titers)
- IgM aCL (moderate/high titers)
- positive lupus anticoagulant test (LAC)

Antiphospholipid syndrome - diagnosis

- clinical signs
- laboratory tests

1. lupus anticoagulant (LAC – no senstitivity)
2. anticardiolipin antibody (aCL - no specificity)
3. anti β2 glycoprotein 1 antibody

## Secondary APS - etiology

- systemic autoimmune diseases
- infections
- malignancies

## Secondary APS – autoimmune diseases

- systemic lupus erythematosus
- rheumatoid arthritis
- systemic sclerosis
- morbus Sjögren
- dermatomyositis/polymyositis
- psoriatic arthropathy
- vasculitis (PAN, mPA, mb Behçet...)

## Secondary APS - infections

Bacterial
- syphilis
- tuberculosis
- Lyme disease
- leprosy
- infective endocarditis,
- rheumatic fever (Streptococcus)
- Klebsiella species infections
- Mycoplasma

Viral
- HIV
- CMV
- rubella,
- hepatitis A-B-C
- mumps

Protozoal
- malaria
- toxoplasmosis

## Secondary APS - malignancies

Solid tumors
- lung
- cervix
- prostate

- liver
- thymus
- esophagus
- maxilla
- ovary
- breast

Haematologic malignacies
- myeloid & lymphatic leukemias
- polycythemia rubra vera
- myelofibrosis

Lymphoproliferative diseases
- mb Hodgkin
- non-Hodgkin lymphoma
- lymphosarcoma

Paraproteinemias
- monoclonal gammapathies
- mb Waldenström
- multiple myeloma

Preliminary classification criteria for APS

**Clinical criteria**

1. vascular thrombosis (arterial and/or venous)
2. pregnancy morbidity

**Laboratory criteria**

1. anticardiolipin antibody (aCL)
2. lupus anticoagulant (LAC)

Arthritis Rheum 1999;42:1309-1311.

Pregnancy morbidity associated with APS
(preliminary classification – Sapporo 1999)

- 1 or more unexplained deaths of morphologically normal fetus $\geq 10^{th}$ week of gestation with normal fetal morphology documented by ultrasound or direct examination of the fetus
- 1 or more premature births of morphologically normal neonate $\leq 34^{th}$ week of gestation because of severe preeclampsia or placental insufficiency
- $\geq 3$ consecutive spontaneous abortions before $10^{th}$ week of gestation with maternal anatomic-hormonal -chromosomal and paternal chromosomal causes excluded

Arthritis Rheum 1999;42:1309-1311.

Pregnancy morbidity associated with APS - histopathology

- histology is not specific:

- placental infarctions, necrosis, thrombosis
- spiral artery vasculopathy (acute atherosis, intimal thickening, fibrinoid necrois)
- villus abnormalities cionsistent with hypoxia

- thrombosis & infarction – 82% of placentas from women with aCL and fetal death
  (Ann Rheum Dis 1991;50:553-557)

Pregnancy morbidity associated with APS – clinical presentation

- recurrent miscarriage
- growth retardation
- pre-eclampsia
- HELLP

Management of APS in pregnancy

- preconceptional counseling
- antenatal surveillance and monitoring
- pharmacotherapy during pregnancy
  a. aspirin (- thrombotic history)
  b. LMWH (+ thrombotic history, high risk)
  c. hydroxychloroquin
  d. therapy of main rheumatic disease