

## Anaesthesia recommendations for patients suffering from

### **Antiphospholipid Antibody Syndrome**

**Disease name:** Antiphospholipid Antibody Syndrome (APS)

**ICD 10:** D68.6

**Synonyms:** Antiphospholipid Syndrome (APS)

Antiphospholipid syndrome (APS) is a complex autoimmune disease often connected to systemic lupus erythematosus. Main features are specific antiphospholipid antibodies (aPL), thrombosis (arterial, venous or microvascular) and/or pregnancy complications and failure. The involved antibodies are directed against plasma proteins such as beta-2-glycoprotein1 ( $\beta$ 2GPI) or prothrombin which depends on negatively charged phospholipids. Antibody- $\beta$ 2GPI complexes bind to a variety of receptors on different cell types, including endothelial cells, platelets, monocytes and trophoblasts and may trigger intracellular signalling and inflammatory responses. There is increased expression of tissue factor on monocytes and endothelial cells, interference in protein C anticoagulant pathways, inhibition of fibrinolysis and inhibition of annexin V binding to phospholipids. Pregnancy failure may be due to thrombosis in the placental bed, although alternative mechanism may explain the tendency to very early losses prior to placentation. Clotting tests such as activated partial thromboplastin time (aPTT) and diluted Russell's viper venom test (dRVVT) show a prolonged time for coagulation despite prothrombotic state. Clotting test could be misleading so clinical judgement is mandatory.

---

Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

---



Find more information on the disease, its centres of reference and patient organisations on Orphanet: [www.orpha.net](http://www.orpha.net)

---

## Disease summary

---

APS has been described secondary if there is an associated autoimmune disorder, such as systemic lupus erythematosus (SLE) or rheumatoid arthritis, and primary if not. There is high morbidity and mortality in the patients during perioperative period. The surgical experience with APS patients mainly relies on few case reports describing one or two patients. The risk of thrombosis and bleeding are present in patients with APS. Early institution of anticoagulation with antiplatelets and other anticoagulants is considered as safe treatment.

In addition to thrombosis and pregnancy morbidity, patient with APS may have other clinical associations e.g. Myocardial ischemia/infarction, heart valve disease, thrombocytopenia, ischemic strokes, chorea, livedo reticularis/ racemosa, nephropathy, transverse myelopathy, migraine.

---

## Typical surgery

---

Caesarean section, abortion, dilation and curettage of retained product of conception.

Thrombo-embolectomy.

Heart valve replacement: The link between APS, valvular heart lesions and thrombo-embolic events is not fully elucidated. Various valve lesions have been seen by echocardiography. The irregular thickening of mitral valve followed by aortic valve is the most common finding. There is high morbidity and mortality in the patients with these valve replacements.

---

## Type of anaesthesia

---

General or regional anaesthesia have been used with successful results.

Standard technique of general anaesthesia using depolarizing or non-depolarizing muscle relaxants, inhalation agents and opioids is used. General anaesthesia has been performed as total intravenous anaesthesia. Nitrous oxide can be used, but should be avoided in case with cardiac involvement.

Regional or local anaesthesia can be done with caution. Few authors have reported use of neuroaxial block anaesthesia in these patients without any complication. In the absence of coagulation defects secondary to clotting factors antibodies or platelet abnormalities, the in vitro phenomenon of prolonged APTT alone should not predispose to haemorrhage or be a contraindication to epidural anaesthesia in patient with APS. Insertion of the spinal needle should be delayed for 10-12 h after the initial LMW heparin dose; subsequent doses should be delayed at least 2 h after spinal needle placement or catheter removal. For patients in whom LMW heparin prophylaxis is started post-operatively, the initial dose should also be delayed at least 2 h. However the result of these studies, do not prove that neuroaxial block are safe in the setting as the studies were done on a small numbers of patients.

There is no contraindication for sedation.

Patient is kept well hydrated.

Medications increasing risk of thrombosis (e.g. hydralazine) should be avoided.

Patient require close monitoring for bleeding and thrombotic complications postoperatively.

### **Necessary additional diagnostic procedures (preoperative)**

---

Criteria for defining the antiphospholipid antibody syndrome

Clinical criteria

1. Vascular thrombosis

a. One or more clinical episodes of arterial, venous or small vessel thrombosis

2. Pregnancy morbidity

a. One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation

b. One or more pre-term births of a morphologically normal neonate before the 34th week of gestation because of (1) eclampsia or severe pre-eclampsia or (2) recognized features of placental insufficiency

c. Three or more unexplained consecutive spontaneous miscarriages before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded

Laboratory criteria (positive test on two or more occasions at least 12 weeks apart)

1. Lupus anticoagulant (LA) present in plasma

2. Anticardiolipin (aCL) antibody of IgG and/ or IgM isotype in serum or plasma, present in medium or high titre [ > 40 IgG antiphospholipid units (GPL) or IgM antiphospholipid units (MPL)]

3. Anti-beta 2 GPI antibodies of IgG and/ or IgM isotype in serum or plasma

Antiphospholipid antibody syndrome is present if at least one of these clinical criteria and one of these laboratory criteria are present in patient.

#### Pre-operative assessment

Patient should be carefully questioned about bleeding, thrombosis and immune disorders. Haematological screening must include a complete coagulation profile and antiphospholipid antibodies (aPL) titres. When assessing clinical significance account should be taken of whether the patient has LA, aCL/ anti-  $\beta$ 2GPI, or both and of the isotype and titre in the solid phase tests.

Serial ultrasonographic assessment during antepartum checkup is done for fetal wellbeing.

Cardiac function test including electrocardiography and echocardiography should be performed for evaluating presence of cardiac thrombus and cardiomyopathy. Although rare, but there are chances of intracardiac thrombus and pulmonary embolism.

Lung function test including lung volumes and blood gas analysis should be done to evaluate grade of pulmonary involvement.

## Screening

Patient with unprovoked proximal DVT or PE should be screened for aPL.

We advise screening for APS in all young cardiac patient with history of thrombotic/ embolic events including myocardial infarction, coronary graft occlusion, stent or thrombosis of native or prosthetic heart valves.

Patient with APS should undergo echocardiography examination to look for heart valve disease.

---

### **Particular preparation for airway management**

---

No special recommendations.

---

### **Particular preparation for transfusion or administration of blood products**

---

There may be a higher requirement for blood products in patients with APS during high invasive surgery.

---

### **Particular preparation for anticoagulation**

---

These patients may be chronically anti-coagulated. Oral treatment may be replaced with either unfractionated heparin (UFH) or low molecular weight heparin (LMWH). Treatment should be tailored so that on the day of surgery, the international normalised ration (INR) is normal.

---

### **Particular precautions for positioning, transport or mobilisation**

---

Not reported.

---

### **Probable interaction between anaesthetic agents and patient's long term medication**

---

APS patients are at a very high risk for thrombo-embolic complication in perioperative period in particular following cardiac surgery, which can arises due to....

1. Preoperatively with reversal of anticoagulation
2. Intra-operatively due to inadequate anticoagulation on cardiopulmonary bypass
3. Postoperatively prior to adequate anticoagulation or as a result of catastrophic APS and multi-organ failure.

## Anaesthesiologic procedure

---

There are many other risk factors for thrombosis e.g. hypertension, diabetes mellitus, hyperlipidaemia. These should be treated optimally.

Smoking and sedentary life styles are avoided.

Avoid oral contraceptive pill or oestrogen therapy.

Perioperatively, APS leads to thrombosis which may occur spontaneously or may be precipitated by infection, surgical intervention, any change in anticoagulation therapy or introduction of oral contraceptive pills. High dose anticoagulation suitable for the long term management of these patients presents a major problem in the perioperative period.

General anaesthesia is usually preferred. Although regional anaesthesia is sometime employed.

In case of present cardiac disease avoid nitrous oxide because of cardio-depressant effects. Opiates, propofol and local anaesthetics have been used without any complication. Non-depolarizing neuromuscular blocking agents can be used safely in these patients. Antagonisation of neuromuscular blockade with pyridostigmine or neostigmine seems to be possible.

### Choice of valve in cardiac surgery

For heart valve surgery, reconstructive methods are always preferred as first choice. But in APS, valve inspection revealed tissue destruction, with thickening and vegetation leading to high failure rate if repair is tried. So in majority of patients valve is replaced. Considering younger age at the time of replacement and better prognosis with intensive medical treatment few authors consider mechanical valve. But high INR is required for a mechanical valve and few authors has reported thromboembolic complication even with an INR of 3-4 in APS. Strict and coordinated perioperative control of the anticoagulant therapy must be accomplished.

Tissue valve allows easy managements of oral anticoagulation therapy as it does not require complex monitoring of oral anticoagulation. Therefore we prefer tissue valve in our institute. These allow easy and safe management of thrombo-embolic and bleeding complication which is seen in APLS patients.

### Intra-operative period

Cardiopulmonary bypass (CPB)

It require extensive anticoagulation and close monitoring to prevent clot formation and pump failure.

### Dose of heparin

Intraoperative heparin monitoring during cardiopulmonary bypass surgery can be challenging because APS patients may have elevated baseline ACT level. We use unfractionated heparin (UFH) 400 units / kg body weight and maintain activated clotting time (ACT) more than 450 seconds prior to aortic cannulation. In the presence of heparin antibodies, we use Bivalirudin.

### Monitoring of anticoagulation

Few authors have suggested: doubling the baseline ACT level; obtaining heparin concentrations by protamine titration rather than following ACT levels; performing heparin-ACT titration curves preoperatively to determine patient-specific target ACT levels. Use of factor Xa level to check heparin efficacy is also time consuming, so monitoring is commonly done with measuring ACT. In our clinical experience it has given us safe and successful results. We check baseline ACT level before heparin administration. Thereafter ACT is checked every 30 minutes of heparin administration. We keep ACT more than 450 seconds. Additional doses of heparin are administered as necessary. Heparin concentration of > 3 Units/ ml is assumed sufficient for effective anticoagulation on CPB. Anti-fibrinolytic is avoided as there is theoretical risk of increased thrombotic events.

### Reversal of anticoagulation

At the end we use half dose of protamine to partially reverse heparin effects. We add more protamine in step wise manner till bleeding tendency slows down to acceptable level.

There is no need for prophylactic postoperative ventilation.

---

### **Particular or additional monitoring**

---

Monitor body temperature to avoid shivering and increased oxygen demand.

In case of high-risk surgery, major fluids shifts or advanced disease arterial cannulation for invasive blood pressure measurement and central venous line placement is recommended.

In case of cardiac operation, transesophageal echocardiography is very useful.

---

### **Possible complications**

---

The risk of thrombosis and bleeding are present in patients with APS. This may lead to venous thrombosis, arterial ischaemic stroke and pregnancy morbidity (fetal loss, intrauterine growth retardation, placental insufficiency, preterm delivery). In addition patient may develop myocardial ischemia/infarction, heart valve disease, autoimmune thrombocytopenia, chorea, livedo reticularis/ racemosa, nephropathy, transverse myelopathy, migraine.

Catastrophic APS is an acute onset, life-threatening cause of multi-organ failure. It is a rare condition that may complicate APS.

---

### **Postoperative care**

---

Adequate hydration is advised.

Keep the patient warm.

Avoidance of thrombotic complication by careful anticoagulation treatment is so far the only long-term treatment option for APS patient.

Optimal analgesia and early mobilisation reduces the risk of venous thromboembolism.

We give mechanical thromboprophylaxis including intermittent pneumatic compression or anti-embolism stocking to all patients. Along with, we add pharmacological methods and use aspirin and UFH or LMWH .

Patient can develop thrombosis despite appropriate prophylaxis.

Lifelong anticoagulation is recommended in valve cases. The target INR is high at about 2.5 (target range 2.0-3.0). If patient develop further thrombotic events despite adequate anticoagulation, the dose of warfarin and target INR are increased or antiplatelets are added.

---

### **Information about emergency-like situations / Differential diagnostics**

---

*caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the diseases*

Suboptimal anticoagulation or withdrawal of anticoagulant leads to hypercoagulability state and this can cause catastrophic APS. Treatment of this hypercoagulable state or thrombocytopenia, a common feature of APS, may cause acute onset, life-threatening hemorrhage. This may lead to multi-organ failure.

---

### **Ambulatory anaesthesia**

---

Not reported.

---

### **Obstetrical anaesthesia**

---

Antithrombotic interventions are used to reduce the incidence of pregnancy complications.

Women with recurrent pregnancy loss ( $\geq 3$  pregnancy losses) before 10 weeks gestation should be screened for aPL.

For women with APS with recurrent ( $\geq 3$ ) pregnancy losses, prophylactic heparin and low dose aspirin are recommended during pregnancy and for 6 weeks after the delivery. This reduces the incidence of pregnancy loss. In general, treatment should begin as soon as pregnancy is confirmed. In patients with vascular APS we should stop warfarin and start heparin full dose and low dose aspirin during pregnancy, restarting warfarin 6 weeks post partum or after delivery.

Women with APS should keep taking low dose aspirin after pregnancy.

For women with APS and a history of pre-eclampsia, low dose aspirin is recommended.

Women with persistent aPL with no previous VTE and no other risk factors or fetal indications for LMWH may be managed with close surveillance antenatally but should be considered for LMWH for 7 days postpartum. Women with previous thrombosis and APS should be offered both antenatal and 6 weeks of post-partum thromboprophylaxis

## Literature and internet links

1. Hughes GRV. The antiphospholipid syndrome; ten years on. *Lancet*,1993;342:341-344
2. Gorki H, Malinovski V, Stanbridge RDL. The antiphospholipid syndrome and heart valve surgery. *Europ Jour Cardio-thorac Surg*, 2008;33:168-81
3. Turiel M, Muzzupappa S, Gottardi B, Crema C, Sarzi-Puttini P, Rossi E. evaluation of cardiac abnormalities and embolic sources in primary antiphospholipid syndrome by transesophageal echocardiography. *Lupus* 2000;9:406-12
4. Colli A, Mestres CA, Espinosa G, Plasín MA, Pomar JL, Font J, Cervera R. Heart valve surgery in patients with the antiphospholipid syndrome : analysis of a series of nine cases. 2010;37:154-58
5. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RHWM, DeGroot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A, Vlachoyiannopoulos PG, Krilis SA. Internation consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Throm Haemost* 2006;4:295-306
6. Galve E, Ordi J, Barquinero J, Evangelista A, Vilardell M, Soler-Soler J. Valvular heart disease in the primary antiphospholipid syndrome. *Ann Intern Med*. 1992;116:293-98
7. Keeling D, Mackie I, Moore GW, Greer IA, Greaves M, and British committee for standards in Haematology. Guidelines on the investigation and management of antiphospholipid syndrome. *British J Haematology* 2012;157:47-58
8. Perez-Villa F, Font J, Azqueta M, Espinosa G, Pare C, Cervera R, Reverter JC, Ingelmo M, Sanz G. Severe valvular regurgitation and antiphospholipid antibodies in systemic lupus erythematosus: a prospective, longterm, follow-up study. *Arthritis Rheum* 2005;53:460—7
9. Rawat RS, Mehta Y, Saxena P, Juneja R, Bhan A. Double valve replacement in a patient with antiphospholipid antibody syndrome. *Annals Cardiac Anaesth* 2011;14:235-236
10. East CJ, Clements F, Mathew J, Slaughter TF. Antiphospholipid syndrome and cardiac surgery: management of anticoagulation in two patients. *Anesth Analg* 2000;90:1098—101
11. Sheikh F, Lechowicz A, Setlur R, Rauch A, Dunn H. Recognition and management of patients with antiphospholipid antibody syndrome undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 1997;11:764—6
12. Lim W, Crowther MA, Eikelboom MS. Management of antiphospholipid antibody syndrome, a systematic review. *American Medical Association* 2006;25:1050-57
13. Rawat R S, Dehran M. Anaesthetic management of a pregnant patient with antiphospholipid antibody syndrome for emergency caesarean section. *Internation journal of obstetric anesthesia* 2003;12:311.

---

**Last date of modification: February 2015**

---

*These guidelines have been prepared by:*

**Authors**

**Yatin Mehta**, Anaesthesiologist, Medanta Institute of Critical Care & Anesthesiology,  
Medanta The Medicity, Gurgaon, Haryana, India  
[drmayankvats@gmail.com](mailto:drmayankvats@gmail.com)

**Mayank Vats**, Senior specialist, Pulmonologist, Intensivist and sleep physician, Rashid  
Hospital, Dubai Health Authority, Dubai, United Arab Emirates (UAE)  
[drmayankvats@gmail.com](mailto:drmayankvats@gmail.com)

**RS Rawat**, Anesthesiologist, Medanta, MEDICITY, Gurgaon, Medanta The Medicity,  
Gurgaon, Haryana, India

**Peer revision 1**

**Adriana Danowski**, Hospital Federal dos Servidores do Estado, Rio de Janeiro, RJ, Brazil  
[adrid@globo.com](mailto:adrid@globo.com)

**Peer revision 2**

**David Keeling**, Haematologist, UK  
[david.keeling@ndm.ox.ac.uk](mailto:david.keeling@ndm.ox.ac.uk)

*Please note that this guideline has not been peer-reviewed by an anaesthesiologist but by two disease experts.*

---