orphanaesthesia

Anaesthesia recommendations for

MYH9-related disease (MYH9-RD)

Disease name: MYH9 related disease (OMIM 600208)

ICD 10: D69.4

Synonyms: May-Hegglin anomaly, Epstein syndrome, Fechtner syndrome, Sebastian syndrome, MYH9 related thrombocytopenia, MYH9 related syndrome, MYH9-related syndromic thrombocytopenia, MYH9-related disorder, MYH9-related disease (MYH9-RD).

With more than 300 families reported in the literature, MYH9-RD is the most frequent form of inherited thrombocytopenia (1,2). It encompasses four dominant disorders previously considered as distinct disorders (see synonyms). MYH9-RD is then phenotypically variable and is characterized by a congenital macrothrombocytopenia as well as characteristic leucocyte inclusions (Döhle bodies) in all patients. Some patients may develop additional clinical features such as cataracts, hearing loss and/or progressive kidney disease. This is a rare autosomal dominant inherited disorder caused by mutations of the MYH9 gene encoding for the heavy chain of non-muscle myosin-IIA (myosin9). The bleeding tendency is broadly related to the level of platelet count. The main anesthetic concerns in the management of patients with MYH9-RD are the development of a strategy to reduce haemorrhagic complications and the screening of associated disorders, particularly renal and hepatic impairment. The possibility of performing neuraxial anaesthesia will depend on platelet levels and normal platelet function.

Disease summary: In 1909, May observed that the blood smear of a woman referred to him showed many leukocytes which contained one or several pale blue inclusions bodies (3). Thirty-six years later, Hegglin described in three members of the same family the combination of a thrombocytopenia with giant platelets and the presence of Döhle like bodies in their neutrophils (4). The name “May-Hegglin anomaly” was used in a case report by Scholer et al. that Hegglin commented as identical to his own report. Thereafter the conjoined eponym “May-Hegglin anomaly” was used.

The disease locus was mapped to chromosome 22q12.3-q132 by linkage analysis (5,6). The gene responsible for this disorder was identified as MYH9, which encodes a large cytoplasmic protein (NMMHC-IIA), expressed in many different tissues including blood cells, kidney, cochlea, hepatocytes. This protein regulates the cytoskeleton and acts as a key component of the activities that drive cell migration, cell-cell interaction and cell matrix adhesion. The pathogenesis of thrombocytopenia is mainly secondary to defective proplatelet formation by increased contractibility.

Several other inherited disorders that were previously considered to be separate entities (see synonyms) were in fact caused by mutations in the MYH9 gene. Therefore the name MYH9-related disease or MYH9 disorder has been proposed (7). To date, over 80 different mutations have been identified (8,9). The majority of patients are heterozygous for missense mutations and some patients for nonsense or frameshift or deletions or duplications.

Importantly, 35% of MYH9-RD cases are sporadic and in half of them a de novo mutation is confirmed by molecular testing in parents.

The thrombocytopenia is characterized by large platelets (ie 40% of platelets > 3.9 µm in diameter) and a platelet count <150x109/L, both detected from birth. Sometimes the platelet count decreased may be more severe < 30x109/L. Platelet aggregation, serotonin release, clot retraction are more often normal or slightly altered. Döhle bodies stained by May-Grunwald-Giemsa are present in 42-84% of individuals with MYH9-RD but detectable in all affected patients by immunofluorescence labelling for non-muscle myosin heavy chain IIA protein of granulocytes (1).

The severity of bleeding is broadly related to the platelet count but most patients have a low haemorrhagic score as defined by the International Society of Thrombosis and Haemostasis bleeding assessment tool (ISTH/BAT) (10,11). The prevalence of mucocutaneous bleeding was significantly higher for patients with head domain mutations of the myosin 9 (12). So, the diagnosis may wait until adulthood as they are at risk to develop renal failure, deafness or cataract in early or middle life. Easy bruising, spontaneous mucocutaneous bleedings, excessive bleedings after haemostatic challenges or treatment with drugs interfering with platelet function are manifestations of thrombocytopenia. In some rare patients with severe bleeding due to menorrhagia or intracranial bleeding, platelet transfusions should be used. Nevertheless, recent progress in the preoperative management by using thrombopoietin (TPO) mimetics must be noticed and are an interesting alternative in adults and children (13,14,15,16).

Differential diagnosis includes other macrothrombocytopenias (MTP) such as Bernard-Soulier syndrome (OMIM 213200/153670) or ACTN1(OMIM 615193) or ITGA2B ITGB3 (OMIM187800) or TUBB1(OMIM613112) or DIAPH1(OMIM124900) related thrombocyte-penias (17).

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

Surgical procedures that are specific to MYH9-RD can be related to the associated syndromes. These are: cochlear implantation, ophtalmic surgery, renal transplantation (18,19,20). All other types of surgical procedures may be performed in these patients (21,22,23,24). Ideally, all patients should be managed, in particular during pregnancy, by a multidisciplinary team combining several experts in anaesthesia, haemostasis and obstetrics during pregnancy.

Several important points should be kept in mind for the anaesthesiologist for the management of a patient: is the decision for the surgical procedure elective or in emergency? Is it necessary to obtain an urgent increase in platelet count for patients at high risk of bleeding? Ensure that the most appropriate expert advices have been obtained.

Type of anaesthesia

No explicit recommendations or guidelines have been published for patients with haemostatic disorders, in particular inherited platelet disorders.

Potential renal or hepatic damage should be integrated into the pharmacokinetics of anaesthesia agents used.

Before performing neuroaxial or peripheral nerve blocks and in order to prevent the risk of haematoma secondary to regional anaesthesia, there should be taken into account the severity of the thrombocytopenia, the coagulation status (platelet functions), the presence of clinical bleeding and the benefit-risk balance of the procedure for a given patient. It is important to underline that an exact optical and manual platelet count must be requested when the haematological analysers used are not able to take into account the presence of giant platelets (24).

Neuro-axial anaesthesia was successfully performed in several studies with platelet counts at least 80x109/L (25, 26). Spinal or epidural anaesthesia are generally safe when the platelet count is at least equal to 80x109/L but in some reports they have been performed in women with a platelet count under 50x109/L (27). Nevertheless, there is insufficient published evidence to make recommendations for lower platelet counts presently. For this reason, in accordance with published recommendations (28,29), loco-regional anaesthesia procedures remain possible if platelet functions are normal and their count ≥ 80x109/L. For patients with platelet counts less than 75x109/L, an individual decision based on benefits and risks must be made (30).

No contraindication for sedation or certain pain management methods are known at the present time but it has been recommended that repeated use with NSAIDs should be administered carefully in patients with MYH9-RD.

Necessary additional pre-operative testing (beside standard care)

Besides the necessity to obtain a correct platelet count in the preoperative or pre partum period, it is necessary also to obtain data on platelet functions i.e platelet aggregation and platelet secretion when the level of thrombocytopenia allows these investigations. It should be noted that for the majority of patients these functions are normal but it is important to

verify this point and to exclude for example acquired additive abnormalities. These functions may be tested by different methods due to the level of the platelet count. If this count is above 80x109/L, the aggregometry method can be used; under this level, we recommend to test platelet function by flow cytometry, a very interesting method that requires a low quantity of blood and can be used not only for adults but also for children. Another alternative which might be beneficial in the future for decisions in cases of surgical or obstetrical emergencies is to perform preoperative thromboelastography (TEG) (30), but so far no consensus has been obtained and no official recommendation can be made.

Assessment of renal function and hepatic function is indicated whatever patient age. Patients may be asked whether they present a hearing loss and whether or not they have a cataract.

Particular preparation for airway management

Bleeding after airway trauma and intubation is a theoretical risk in these patients but has not been reported up to now. No consensus has been published concerning the selection of therapeutic method and no specific guideline about platelet count necessary to prevent the trauma of airway is available at the moment. In case of difficult intubation and particularly if platelet count is at least 50x109/L, the use of fiberscope or video laryngoscope may reduce the risk of bleeding.

Particular preparation for transfusion or administration of blood products

Transfusion of platelet concentrates may be helpful in immediate preoperative period or at the very beginning of the surgical procedure. In some reports, HLA matched platelet transfusions were used as a better option, so it's necessary to treat these patients in surgical or obstetrical centers connected with blood banks allowing a rapid access to these blood products.

Similarly to previous guidance provided for ITP (31), the following platelet counts could be necessary for the different procedures; simple dental extraction or regional dental block: >30x109/L; complex extractions: > 50x109/L; - minor surgery > 50X109/L; major surgery such as neurosurgery, renal transplantation >100x109/L (32,33).

If the surgery is not urgent, we recommend to administrate TPO mimetics either each day per os or by one sub cutaneous injection per week. The increase of platelet count is detected from 2 to 4 weeks after the beginning of this treatment which may avoid platelet transfusion (12,13,14,15). If indicated during the perioperative period, treatment is generally started 4 weeks before the surgery and the minimal platelet count to reach is 50 x 109/L but depends also of the type of surgery (see above). The platelet level and liver enzymes must be monitored every week. Duration will be adjusted to the haemorrhagic risk in the post-operative period: platelet count will return to its baseline rate one to three weeks after the end of treatment.

Particular preparation for anticoagulation

MYH9-RD thrombocytopenia does not protect against thromboembolic complications (34,35,36) that can also be present after surgery in the absence of adequate anti-thrombotic prophylaxis. So prophylactic anticoagulation must be administrated when needed in the

postoperative period of surgeries with high risk of thrombosis and mechanical prophylaxis (compression stocking) should be also considered.

Particular precautions for positioning, transportation and mobilisation

No special precaution for positioning, transport or mobilisation is recommended. Any trauma must be avoided.

Interactions of chronic disease and anaesthesia medications

All medication interfering with platelet function: aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) or antiplatelet agents must be avoided.

At the opposite, antifibrinolytic agents such oral or IV tranexamic acid and epsilon aminocaproic acid may be used usefully in preventing recurrent bleeding in these patients and in certain dental or surgical procedures (37).

Anaesthetic procedure

All kind of general anaesthesia methods may be used for emergency and elective surgeries in patients with MYH9-related disease.

Particular or additional monitoring

Additional monitoring is dependent on the type of surgery and the risk of bleeding. To consider central venous catheter in patients at great risk of bleeding during surgery, the platelet count must be > 50-60x109/L with normal platelet function. If bleeding is expected, haemodynamic monitoring and cell salvage has to be anticipated as well as a constant connection with blood bank and delocalized haemoglobin and coagulation follow-up. In cases of renal or hepatic dysfunction, a strict non-invasive or semi invasive hemodynamic monitoring should be anticipated preoperatively for the surgery and the postoperative period.

Possible complications

The risk of fatal bleeding is very low but this risk is, as in the general population, increased in old patients, patients with a previous history of bleeding or patients with other associated comorbidities: hypertension, liver cirrhosis, cardiovascular events inducing the use of anti-platelet agents or anticoagulants.

Fatal bleeding complications in child and adults have never been reported to date even if the bleeding tendency is associated with a lower platelet count in bleeders than in non-bleeders. (9).

Complications due to the use of TPO mimetics must be known also: risk of thrombosis described in some rare reports, and a platelet count must be performed one month after the end of the treatment (16).

Post-operative care

Postoperative care is necessary and dependent on the known risk of bleeding of the surgery and if the patients are known to have a high bleeding score. In some surgeries as renal transplantation or neurosurgery, a platelet count equal or higher than to 100x109/L in the pre- and post-operative periods has been recommended (32,33). Then, all these clinical data induce the necessity of a close attention for platelet count and bleeding in the postoperative period during 6-7 days for minor surgery to 14 days for major surgery. We think that all these patients require also a close follow-up after being released from the hospital.

As previously mentioned, MYH9-RD macrothrombocytopenia does not protect against postoperative venous thromboembolism, and patients should be considered for routine postoperative thromboprophylaxis in situations with a high risk of thrombosis.

Disease-related acute problems and effect on anaesthesia and recovery

As with other patients, emergency situations may occur before or after surgery itself. In the event of uncontrolled bleeding, platelet transfusion should be considered. Possible therapeutic approaches might include recombinant factor VIIa (rFVIIa) but no reports have been published with this alternative.

Desmopressin has been tested in MYH9-RD with success (38) but it's always necessary, due to the variability of the biological effects observed from one patient to another, to test the therapeutic response before using it. So, desmopressin is only indicated in surgery with moderate or low risk of bleeding and in which a correction of primary haemostasis is necessary for a short time. Desmopressin cannot be used in emergency.

The particular case of peri partum haemorrhages is discussed below.

Ambulatory anaesthesia

There are no reports concerning ambulatory anaesthesia in patients with MYH9-RD but we think that with some patients with a low bleeding risk, the surgery can beneficiate from ambulatory procedures.

Obstetrical anaesthesia

The management of patients with inherited platelet disorders (IPD) raises questions not only for the pregnant woman but also for the neonate in the absence of any established recommendations. Nevertheless, recent retrospective studies provide some insights into pregnancy monitoring, childbirth and peri partum period.

It is well establish that platelet count decreases during pregnancy, and interestingly, the large analysis of 339 pregnancies in 181 women with 13 different forms of IPD (39), indicates that the bleeding complications were significantly increased for women with a platelet count less than 40X109/L before delivery, <50X109/L platelets at delivery and also for women with haemorrhagic complications observed during previous surgical procedures. Women with no bleeding and platelet count of at least 80x109/L are at low risk for bleeding and do not require platelet transfusion for labour or delivery. It is noteworthy that this report covered 185 pregnancies for patients with MYH9-RD combining also MTP and hearing loss; normal vaginal delivery was observed for 94 cases with a median platelet count of 60X109/L (34-80X109/L) and for 34 deliveries spinal or epidural analgesia was performed. For the patients with the lowest platelet count, prophylactic platelet transfusion was performed.

A frequent improvement of haemorrhagic symptomatology is observed during pregnancy and can be investigated by questioning and repeating platelet function studies (flow cytometry). Platelet concentrates must be available on site for delivery: preferentially HLA compatible platelets may be prepared before delivery to avoid immunisation and long term platelet transfusion inefficiency. There is no indication for systematic prophylactic platelet transfusion due to the phenotypic variability. A multidisciplinary discussion should be conducted on a case-by-case basis, depending on platelet count, platelet function at the end of pregnancy and mode of delivery.

Management of delivery is similar to other acquired or inherited platelet disorders. In case of post partum haemorrhage (PPH) the algorithm for the management of PPH will be adapted with early platelet transfusion.

Neuraxial anaesthesia remains contraindicated when platelet count is <75-80x109/L (28,29,31) but has been performed in some patients with lower platelet count (27,40).

Caesarean sections are possible with platelet transfusion required often, especially if there are abnormal platelet functions and/or a high bleeding score and/or if the platelet count is less than 50X109/L. Recently, several reports highlighted the use of TPO mimetics during pregnancy in women with inherited or acquired thrombocytopenia (41,42). In these reports, eltrombopag has been used if benefits outweighed risks. Side effects are rare but maternal thrombocytosis and hepatotoxicity may occur. This possibility opens new prospects in treatment of pregnant women with MYH9-RD, particularly those with very low platelet counts, and reduces the potential risks associated with repeated platelet transfusions. In IPD, we suggest to start this specific treatment at the beginning of the last month of pregnancy because this time is far from the embryonic period. Nevertheless, it is assigned to pregnancy category C by the Food and Drug Administration (FDA) and controlled studies in pregnancy are lacking.

The perinatal period is an important time in the management of bleeding risk in women and newborns. A platelet count evaluation is essential in the woman and in the newborn and the systematic research of intra cranial haemorrhage by echography should be programmed also in the neonate. In Noris' study two neonates of pregnant women with MYH9-RD died of cerebral haemorrhage and the authors suggest that the infants delivered vaginally by severely thrombocytopenic women with MYH9-RD must be considered at risk of intracranial bleeding (39). We suggest also to preventively administrate systematically platelet concentrates to neonates with a severe thrombocytopenia.

Follow up of the mother after birth is also essential due to the possibility of post partum bleeding appearing as soon as one week or also later after the delivery (43).

References

1. Savoia A, Pecci A. MYH9-related disorders: in Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Armemiya A, editors. Gene Reviews [internet]. Seatte (WA): University of Washington, Seattle; 1993–2018. 2008 Nov 20 [updated 2015 Jul16]
2. Balduini CL, Melazzini F, Pecci A. Inherited thrombocytopenia-recent advances in clinical and molecular aspects. Platelets 2017;28:3–13
3. May R. Leukocytoteneinschlüsse. Dtsch Arch Klin Med 1909;96:1-6
4. Hegglin R. Gleichzeitige konstitutionelle Veränderungen an neutrophilen und thrombocyten. Helv Med Acta 1945;12:439–440
5. Kunishima S, Kojima T, Tanaka T, Kamiya T, Ozawa K, Nakamura Y, Saito H. Mapping of a gene for May-Hegglin anomaly to chromosome 22q. Hum Genet 1999;105:379–383
6. Martignetti JA, Heath KE, Harris J, Bizzaro N, Savoia A, Balduini CL, Desnick RJ. The gene for May-Hegglin anomaly localizes to a <1-Mb region on chromosome 22q12.3-13.1 Am J Hum Genet 2000;66:1449–1454
7. Seri M, Cusano R, Gangarossa S, Caridi G, Bordo D, Lo Nigro C, et al. Mutations in MYH9 result in the May-Hegglin anomaly, and Fechtner and Sebastian syndromes. The May-Hegglin/Fechtner Syndrome Consortium. Nat Genet 2000;26:103–105
8. Pecci A, Ma X, Savoia A, Adelstein RS. MYH9: structure, functions and role of non-muscle myosin IIA in human disease. Gene 2018;664:152–162
9. Saposnik B, Binard S, Fenneteau O, Nurden A, Nurden P, Hurtaud-Roux MF, et al. French networks; Mutation spectrum and genotype-phenotype correlations in a large French cohort of MYH9-related disorders. Mol Genet Genomic Med 2014;2:297–312
10. Rodeghiero F, Tosetto A, Abshire T, et al. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. J Thromb Haemost 2010; 8:2063–2065
11. Elbatarny M, Mollah S, Grabell J, Bae S, Deforest M, Tuttle A, et al. Normal range of bleeding scores for the ISTH-BAT: adult and pediatric data from the merging project. Haemophilia 2014;20:831–835
12. Savoia A, De Rocco D, Pecci A. MYH9 gene mutation associated with bleeding. Platelets 2017;28:313–315
13. Pecci A, Barozzi S, d'Amico S, Balduini CL. Short term eltrombopag for surgical preparation of a patient with inherited thrombocytopenia deriving from MYH9 mutation. Thromb Haemost 2012b;107:1188–1189
14. Gröpper S, Althaus K, Najm J, Haase S, Aul C, Greinacher A, Giagounidis A. A patient with Fechtner syndrome successfully treated with romiplostim. Thromb Haemost 2012,107:590–591
15. Favier R, Feriel J, Favier M, Denoyelle F, Martignetti JA. First successful use of eltrombopag before surgery in a child with MYH9-related thrombocytopenia. Pediatrics 2013;132:e793–795
16. Rodeghiero F, Pecci A, Balduini CL. Thrombopoietin receptor agonists in hereditary thrombocytopenias. J Thromb Haemost 2018, 16:1700–1710
17. Favier R, Raslova H. Progress in understanding the diagnosis and molecular genetics of macrothrombocytopenias. Br J Haematol 2015,170(5):629–639
18. Pecci A, Verver EJ, Schlegel N, Canzi P, Boccio CM, Platokouki H, et al. Cochlear implantation is safe and effective in patients with MYH9-related disease. Orphanet J Rare Dis 2014b;9,100:1–9
19. Min SY, Ahn Hj, Park XW and Kim JW. Successful renal transplantation in MYH9-related disorder with severe macrothrombocytopenia: first report in Korea. Transplantation Proceedings 2014;46: 664–666
20. Hashimoto J, Hamasaki Y, Yanagisawa T, Sekine T, Aikawa A, Shishido S. Successful kidney transplantation in Epstein syndrome with antiplatelet antibodies and donor specific antibodies: a case report. Transplantation Proceedings 2015;47:2541–2543
21. Sehbai AS, Abraham J, Brown V. Perioperative of a patient with May-Hegglin anomaly requiring craniotomy. Am J Hem 2005;79:303–308
22. Eichel Y, Tornos LM, Squites JE. Preoperative use of platelets in a 6-year-old with acute appendicitis and a myosin heavy chain 9-related disorder: a case report and review of literature. Transfusion 2016;56:349–353

23. Orsini S, Noris P, Bury L, Heller PG, Santoro C, Kadir RA, et al. Bleeding risk of surgery and its prevention in patients with inherited platelet disorders. Haematologica 2017;102:1192–1203
24. Kumemura M, Omae T, Kou K, Sakuraba S, Niimi N, Kunishima S. Anesthetic management without perioperative platelet transfusion for cervical laminectomy and laminoplasty in a case of May-Hegglin anomaly. J Anesth 2018;32:641–644
25. Choi S, Brull R. Neuroaxial techniques in obstetric and non obstetric patients with common bleeding diatheses. Anest Ana 2009;109:628–660
26. Gernsheimer T, James AH, Stasi R. How I treat thrombocytopenia in pregnancy. Blood 2013;121:38–47
27. Fishman ER, Connors JM, Camann WR. Anesthetic management of seven deliveries in three sisters with the May-Hegglin anomaly. Anesth Ana 2009;108:1603–1605
28. American College of Obstetricians and Gynecologists' Committee on Practice Bulletin Thrombocytopenia in pregnancy. Obstet Gynecol 2016;128:e43–e53
29. French Society of Anesthesiology. Guidelines. Neuroaxial anaesthesia in adults. Ann Fr Anaest Rea 2007;26:720–752
30. Huang J, McKennay N, Babins N. Utility of thromboelastography during neuraxial blockade in the parturient with thrombocytopenia. AANA Journal 2014; 82:127–130
31. British Committee for standards in Haematology. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003;120:574–596
32. Palandri F, Zoli M, Polverelli N, Noris P, Sollazzo D, Catani L, et al. MYH9-related thrombocytopenia and intracranial bleeding: a complex clinical/surgical management and review of the literature. Br J Haematol 2015;170:729–731
33. Hashimoto J, Hamasaki Y, Takahashi Y, Kubota M, Yanagisawa T, Itabashi Y, Muramatsu M, et al. Management of patients with severe Epstein syndrome: a review of four patients who received living donor renal transplantation. Nephrology 2018;13. DOI:10.1111/nep.13253.[Epub ahead of print]
34. Selleng K, Lubenow LE, Greinacher A, Wartenkin TE. Perioperative management of MYH9 hereditary macrothrombocytopenia. Eur J Haem 2007;79:213–218
35. Kerros H, Roule V, Ivascau C, Labombarda F. Management of May-Hegglin anomaly referred for coronary artery bypass. Platelets 2011;22:471–472
36. Girolami A, Sambado L, Bonamigo E, Vettore S, Lombardi AM. Occurrence of thrombosis congenital thrombocytopenic disorders: a critical review of the literature. Blood Coagul Fibrinolysis 2013;24:18–22
37. Althaus K, Greinacher A. MYH9-related platelet disorders: strategies for management and diagnosis. Transf Med Hemother 2010;37:260–267
38. Coppola A, DiMinno G. Desmopressin in inherited platelet function. Haemophilia 2008;14:31–39
39. Noris P, Schlegel N, Klersky C, Heller PG, Civashi E, Pujol-Moix N, et al. Analysis of 339 pregnancies in 181 women with 13 different forms of inherited thrombocytopenia. Haematologica 2014b;99:1387–1394
40. Garcia Vallejo G, Cabellos M, Kabiri M, Fraile JR, Cuesta J. Anaesthetic implications in a pregnant patient with an extreme thrombocytopenia due to a May-Hegglin anomaly: general or regional anaesthesia? Rev Esp Anesthesiol Reanim 2014;61:460–465
41. Favier R, De Carne C, Elefant E, Lapusneanu R, Gkalea V, Rigouzzo A. Eltrombopag to treat thrombocytopenia during last month of pregnancy in a woman with MYH9 related disease: a case report. AA Pract 2018;10:10–12
42. Kong Z, Qin P, Xiao S, Zhou H, Li H, Yang R et al. A novel recombinant human thrombopoietin therapy for the management of immune thrombocytopenia in pregnancy. Blood 2017;130:1097–1103
43. Hussein BA, Gomez K, Kadir R. May-Hegglin anomaly and pregnancy: a systematic review. Blood Coagul Fibrinolysis 2013,24:554–561.

Date last modified: June 2019

This recommendation was prepared by:

Author(s)

Remi Favier, Haematologist, French reference centre for platelet disorders, Armand Trousseau Hospital, 75012 Paris, France

Agnes Rigouzzo, Anaesthesiologist, Anaesthesiology and Intensive Care Department, Armand Trousseau Hospital, 75012 Paris, France
Agnes.rigouzzo@aphp.fr

Co-authors:

Federica Piana, Anaesthesiologist, Anaesthesiology and Intensive Care Department, CHU Lyon, France

Nicolas Louvet, Anaesthesiologist, Anaesthesiology and Intensive Care Department Armand Trousseau Hospital, 75012 Paris, France

Disclosure(s) The authors have no financial or other competing interest to disclose. This recommendation was unfunded.

This recommendation was reviewed by:

Reviewer 1

Anne-Sophie Ducloys-Bouthors, Anaesthesiologist, Department of Anesthesiology and Critical Care Medicine, Lille University Hospital, Lille, France
anne-sophie.bouthors@chru-lille.fr

Reviewer 2

Paquita Nurden, Haematologist, founder of the French Reference Center for Inherited platelet diseases, Scientific advisor, Liryc Institute, Pessac, 33600, France
Paquita.nurden@gmail.com

Disclosures The reviewers have no financial or other competing interest to disclose.