NATIONAL BLOOD CENTRE
KUALA LUMPUR

GUIDELINES FOR THROMBOPHILIA TESTING

INDICATED FOR THROMBOPHILIA SCREENING:

Lupus Anticoagulant / ACA / Anti-B2GP1:

1. In the presence of unprovoked both arterial and venous thrombosis

2. Unexplained arterial thrombosis (young stroke or Myocardial Infarction) with no risk factors & age <50 year old

3. ≥ 3 unexplained miscarriage <10 weeks gestation

4. 1 or more unexplained foetal death >10 weeks gestation

5. Premature birth with normal morphology <35 weeks gestation due to severe pre-eclampsia or IUGR

6. Patients who have unprovoked Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE) if plan to stop medication

Heritable Thrombophilia Testing:

1. Patients <40 years of age who have unprovoked DVT or PE and had first degree relative who have DVT or PE and plan to stop medication

2. Neonates and children with purpura fulminans should be tested urgently for Protein C (PC) & Protein S (PS)

3. Adults who develop skin necrosis in association with VKAs, suggest to test PC and PS after stop treatment

4. If a women contemplating estrogen use OR pregnancy has a first degree relative with VTE and a known hereditary thrombophilia, test for thrombophilia if the result would change the decision to use estrogen/VTE prophylaxis during pregnancy

Note : thrombosis prone families (2 symptomatic family members)

UNCERTAIN PREDICTIVE VALUE FOR RECURRENCE

1. Test for heritable thrombophilia after first episode of cerebral vein thrombosis

2. Test for heritable thrombophilia after first episode of intra-abdominal vein thrombosis

3. SLE without history of thrombosis / pregnancy morbidities

NOT INDICATED FOR THROMBOPHILIA SCREENING:

1. Patients who plan for continuing anticoagulant treatment

2. Patients who had provoked VTE

3. Asymptomatic people who had first degree relative of DVT, PE or thrombophilia

4. Do not offer heritable thrombophilia testing on patients who had an arterial thrombosis (young stroke or myocardial infarction) including paediatric stroke

5. Indiscriminate testing for heritable thrombophilia test on unselected patients with first episode of venous thrombosis

6. Patients with CVC related venous thrombosis or unselected patients with upper limb thrombosis

7. Patients with retinal vein occlusion

8. Women with hyperstimulation ovarian syndrome

9. Hospitalised patients to identify risk of acquired venous thrombosis

10. During acute episode of thrombosis & pregnancy

11. Patients on anticoagulant - should be discontinued as below :
    a. Warfarin: suggest to send 2 weeks after discontinuation
    b. UFH: suggest to send 24 hours post dose
    c. LMWH: suggest to send 24 hours post dose (min. 12 hrs)
    b. DOAC: suggest to send 72 hours post dose

References :

1. British Journal of Haematology : Guidelines on The Investigation & Management of APS 2012; 157:47-58

2. British Journal of Haematology : Clinical Guidelines for Testing for Heritable Thrombophilia 2010:149:209-220

3. Journal of Thrombosis & Thrombolysis : Guidance for the Evaluation & Treatment of Hereditary & Acquired Thrombophilia 2016; 41:154-164

4. Clinical Practice Guideline in Prevention & Treatment of Venous Thromboembolism, 2013

5. European Journal of Rheumatology : The Clinical significance of APLS in SLE 2016; 3:75-84

6. ISTH: False-negative or false positive: Laboratory diagnosis of Lupus Anticoagulant at the time of commencement of anticoagulant: a rebuttal 2011;9:1435 -1436

7. IJLH: Frequent false-positive results of Lupus Anticoagulant tests In plasmas of patients receiving the new oral anticoagulants & Enoxaparin 2013; 36:144 - 150

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Pusat Darah Negara
Kuala Lumpur
(No. Pendaftaran MPM: 32736)
23/10/18

PUSAT DARAH NEGARA
NATIONAL BLOOD CENTRE
JALAN TUN RAZAK
50400 KUALA LUMPUR
MALAYSIA

Telefon : 603 - 2613 2688
Faksmili : 603 - 2698 0362
Laman Web : www.pdn.gov.my

Rujukan : PDN.100-1/7/3 (2)
Tarikh : 8 hb. Nov. 2018

SENARAI EDARAN SEPERTI DI LAMPIRAN

YBhg. Datuk / Dato' / Datin / Dr. / Tuan / Puan,

GARISPANDUAN PEMPROSESAN & PENGHANTARAN SPESIMEN UJIAN KOAGULASI & THROMBOPHILIA KE PUSAT DARAH NEGARA

Dengan segala hormatnya saya merujuk kepada perkara di atas.

2. Untuk pengetahuan Y.Bhg. Datuk / Dato' / Datin / Dr./ Tuan / Puan pihak Pusat Darah Negara (PDN) menerima specimen yang telah diproses iaitu plasma untuk ujian tersebut di atas dari hospital seluruh Malaysia kecuali hospital di Lembah Kelang dimana mereka boleh menghantar specimen darah yang mana masa pengambilan specimen ke PDN untuk diproses mesti dalam tempoh 4 jam.

3. Mengikut garispanduan standard penghantaran sampel untuk ujian Koagulasi & Thrombophilia mestilah dalam keadaan sejuk beku (*frozen*) untuk menjamin kualiti sampel dan ujian yang akan dihasilkan. Walaubagaimanapun kebanyakan sampel plasma yang diterima oleh PDN adalah dalam keadaan *thawed.* Oleh kerana ujian-ujian tersebut di atas dijalankan secara *batch* maka pihak makmal PDN perlu menyimpan semula sampel plasma tersebut dalam keadaan sejuk beku sehingga tempoh ujian dijalankan dan ini memerlukan sampel di *thaw* semula (*repeated thawing*) dan ini boleh menjejaskan keputusan ujian-ujian tersebut.

4. Sehubungan dengan ini kami memohon supaya pihak YBhg. Datuk / Dato' / Datin / Dr. / Tuan / Puan dapat memastikan sampel plasma yang dihantar ke PDN dalam keadaan sejuk beku (*frozen*) untuk memastikan penghasilan keputusan ujian yang tepat. Ini juga sejajar dengan tindakan pembetulan sebagai penambahbaikan oleh pihak PDN terhadap penemuan audit oleh pihak Jabatan Standard Malaysia pada April 2017. Pihak PDN menyarankan penggunaan "*dry ice*" semasa penghantaran specimen ke PDN untuk memastikan sampel diterima dalam keadaan sejuk beku.

5 Bersama-sama ini dilampirkan Garispanduan seperti di bawah untuk dipatuhi dan sebagai rujukan;

5.1 Garispanduan Pemprosesan & Penghantaran Specimen ke PDN

5.2 Garispanduan Penolakan Sampel Ujian-Ujian Hemostasis

5.3 Garispanduan Permohonan Penyaringan Thrombophilia

6. Dilampirkan bersama-sama ini juga ialah statistik penolakan specimen yang ditolak sepanjang 2017 untuk rujukan YBhg. Datuk / Dato' / Datin / Dr. / Tuan / Puan. Perhatian dan kerjasama YBhg. Datuk / Dato' / Datin / Dr. / Tuan / Puan adalah dipohon untuk memaklumkan kepada semua PTJ masing-masing mengenai perkara ini.

Sekian, terima kasih.

"BERKHIDMAT UNTUK NEGARA"

Saya yang menjalankan amanah,

(DR. NORYATI BINTI ABU AMIN)
No. Pendaftaran Penuh MPM:31319
Pengarah
Pusat Darah Negara
Kuala Lumpur

s.k. :

1. YBhg. Dato' Dr. Hj. Bahari bin Dato' Tok Muda Hj. Awang Ngah
   Pengarah, Bahagian Perkembangan Perubatan
   Kementerian Kesihatan Malaysia.

HAEMOSTASIS UNIT, REFERENCE LABORATORY FOR HAEMOSTASIS AND HAEMATOLOGY
NATIONAL BLOOD CENTRE, KUALA LUMPUR.
(TEL : 03-2613 2610 / 2698)

GUIDELINES FOR SAMPLE COLLECTION / PROCESSING FOR HAEMOSTASIS TESTS

A. THROMBOPHILIA SCREENING

1. Collect blood specimen in **3.2% Trisodium Citrate tube** (light blue cap) as below;
   - 6 to 7 tubes for adult,
   - Minimum of 4 tubes for pediatric 1 year – 12 year old
   - Minimum of 2 tubes for pediatric below 1 year old

   The blood volume to anticoagulant ratio of 9:1 is critical.

2. Blood sample should be processed within **4 hours from the time of collection.**

3. Dispense approximately 0.6 ml of the well-mixed citrated blood into eppendorf tube and freeze it at -30°C to -70°C. The citrated blood sample is for Factor V Leiden and Prothrombin Time 20210A DNA studies.

4. Centrifuge the remaining citrated blood sample at 2000 g x 15 min or 3000 rpm x 10 min.

5. Pipette out the supernatant from each tube into one conical tube.

6. Centrifuge once again at 2500 g x 10 min or 3000 rpm x 10 min (avoid aspirating the buffy coat layer).

7. Aliquot plasma to appropriate tube according to the table :

No	Test	Tubes	Volume	No of tubes		
				Adult	Pediatric 1-12 y.o	Pediatric < 1 y.o
1.	LA	Polyprophylene Tube	2 ml	1 x 2ml	-	-
2.	PC, PS, AT	Polyprophylene Tube	1 ml	1 x 1ml	1 x 1ml	1 x 1ml
3.	ACA, Antiß2GP1	Cryovial Tube	0.1 ml	2 x 0.1ml	-	-
4.	Extra (for APCR, repeat or further tests)	Polyprophylene Tube	1 ml	2 x 1ml	2 x 1ml	1 x 1ml

8. Label each tube with patient's name, i.c number and date of sample collection.

9. Store patient plasma at -30°C to -70°C before send to National Blood Centre.

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B. COAGULATION

10. Collect blood specimen in **3.2% Trisodium Citrate tube** (light blue cap) as below;
    - 5 tubes for adult and pediatric 1 year old and above
    - Minimum of 2 tubes for pediatric below 1 year old

    The blood volume to anticoagulant ratio of 9:1 is critical.

1. Blood samples should be processed within 4 hours from the time of collection.

2. Centrifuge the citrated blood samples at 3000 rpm x 10 min.

3. Aliquot plasma to appropriate tube according to the table:

No	Test	Tubes	Volume	No of tubes	
				Adult	Pediatric < 1 y.o
1.	Basic Coagulation, FVIII & FIX	Polyprophylene Tube	1 ml	1 x 1ml	-
			0.5 ml	-	1 x 0.5 ml
2.	VWF tests	Polyprophylene Tube	1 ml	1 x 1ml	-
			0.5 ml	-	1 x 0.5ml
3.	Other coagulation factors	Polyprophylene Tube	1 ml	2 x 1ml	-
			0.5 ml	-	1 x 0.5ml
4.	Extra (for repeat or further tests)	Polyprophylene Tube	Remaining plasma	2 x 1ml	1 x 0.5ml

4. Label each tube with patient's name, i.c number and date of sample collection.

5. Store patient plasma at -30°C to -70°C before send to National Blood Centre.

C. PACKAGING AND TRANSPORTATION

1. Samples **SHALL BE** transported to National Blood Centre with **dry ice to maintain frozen** throughout transportation and upon receipt in PDN. Sample must be arrived during working office hour. Dispatch the samples to:

   HAEMOSTASIS LABORATORY,
   PUSAT DARAH NEGARA,
   JALAN TUN RAZAK,
   50400 KUALA LUMPUR.

2. Thawed sample upon receipt would be rejected.

3. All samples should be accompanied by ADEQUATE CLINICAL HISTORY and detail particulars of the patient such as NAME, AGE, SEX, I.C NO & RACE. These should be clearly written on the form.

4. Ensure DATE AND TIME SPECIMEN COLLECTION, TEST REQUEST, WARD and HOSPITAL written clearly on the request form.

5. Ensure all test requests shall have requester's name & legal signature.

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MAKMAL RUJUKAN HEMOSTASIS & HEMATOLOGI
PUSAT DARAH NEGARA

GUIDELINES FOR CRITERIA IN REJECTING SPECIMENS IN HEMOSTASIS LABORATORY

The following criteria are used to ensure that the specimens and request forms received by the laboratory meet the basic requirement needed to perform the necessary laboratory tests effectively.

Specimens should be rejected for the following reasons:

A. Blood Specimen

1. Collected in containers other than 3.2 %Trisodium Citrate.
2. Incorrect volume collection (less or greater than 10 % of the expected volume). Should adhere to 1:9 ratio of anticoagulant to blood.
3. Specimen received more than 4 hours from time of collection.
4. Clotted, lysed and lipaemic specimens.
5. No label on the specimen.
6. Patient's particulars on the specimen container do not tally with that in the request form.
7. More than one label (overlap) on the specimen bottles.
8. Illegible writing.
9. Improper handling during transportation.
10. Blood-stained / leaking specimen containers.

B. Plasma Specimen

1. Specimen received in thawed condition*
2. Lysed and lipaemic specimens.
3. Presence of micro clot in plasma received.

* *Ideally plasma specimen should be transported in dry ice in order to maintain in frozen state*

C. Request Form

1. Incomplete patient's particular on the request form. (Haematology / Serology Request Form PDN/HA/QP-01/01 and PER-PAT 301).
2. Absence of Specialist / Medical Officer Identification.
3. Insufficient clinical history.
4. Date and time of specimen collection is not stated.
5. Test required is not stated

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