LabCorp Hypercoagulation Panel (#505443) Interpretation Guide

(preferred reference and reflex values in red)

Lipoprotein (a) ref <31 mg/dL (preferred value) Lp(a) is a genetically driven form of LDL cholesterol that doesn't respond to diet, exercise, or statin drugs but is associated with hypertension, pre-eclampsia, and cardiovascular disease.

- **Lp(a) binds to tPA, preventing the conversion of plasminogen to plasmin. Extra fibrin isn't broken down and accumulates.**
  - **If elevated – stop statin drugs (they increase Lp(a) about 20%) https://pubmed.ncbi.nlm.nih.gov/31111151/**
- **Start extended-release Niacin 500 mg/day with dinner (Enduracin has less flushing than other brands) and Boluoke (Lumbrokinase) 2 capsules together once/day on an empty stomach (give patient the Boluoke instruction sheet).**
- **Boluoke will help lower Lp(a) an additional 20-30% and clear out the fibrin previously accumulated in blood vessels. Only lowering Lp(a) doesn't significantly reduce long term cardiovascular disease risk.**
- **Consider Repatha if the level is greater than twice normal, especially if patient doesn't respond well to Niacin and Boluoke (recheck in 3 months).**

If you recheck Lp(a) as a stand-alone test, the reference range will be <75 since it goes to LabCorp's Burlington location, not Denver. You will need to calculate ratios. For example, if it was about twice as high previously and now only 1.5 times as high as the reference range value, they are responding well to treatment. Continue treating. May need to continue for life.

Homocysteine LabCorp ref 5.0 to 15.0 6-8 umol/L (preferred value since those with MTHFR or Methionine cycle mutations were not excluded from lab reference range).
This is a well-known pro-inflammatory amino acid contributing to clotting and inflammation of blood vessels. Just because elevations are seen in those >60 years doesn't make it acceptable any more than a high blood pressure is acceptable in an older population. Values increasing with age are likely due to poor B12 absorption with lower gastric intrinsic factor production.

- **Those with elevations above 8.0 will need supplementation of B12, B6, folic acid, and sometimes TMG or creatine to reduce their homocysteine. There are several good combination products available.**
- **Low homocysteine levels (<5.0) are also a concern due to inadequate methyl donors, and its contribution to peripheral neuropathy, osteoporosis, and inflammatory bowel disease. SAMe is particularly helpful to provide methyl donors. Treat and recheck in 3 months if out of range.**

Fibrinogen Activity LabCorp ref 160-420 < 325 mg/dL (preferred value) The reference range is skewed to the high end since those with genetic hypercoagulation problems weren't excluded (20% of the general population).

- **This is an indicator of old fibrin build-up.**

- **If patient is a post-menopausal women, male over 60, or has a significant family history of early cardiovascular disease, consider carotid ultrasound and CAC score to determine baseline for cardiovascular disease.**

Alpha-2 Antiplasmin Assay LabCorp ref 80-150 <125 % (preferred value) The reference range included those with the genetics for poor plasmin production (elevated Lp(a) and PAI – 1 4G deletion)

- **Alpha-2 Antiplasmin is the body's most important inhibitor of plasmin. It binds to plasmin, rendering it inactive in degrading**
- **Made by the liver and has a half-life of 3 days**
- **Elevated levels are associated with an increased risk of MI and ischemic stroke**
- **High levels persist in long-COVID patients, hindering the breakdown of the COVID biofilm (a combination of fibrin and amyloid)**
- **Alpha-2 Antiplasmin can be lowered with lumbrokinase dosed according to A2AP levels (See Boluoke dosing chart.)**
- **Recheck level in 4-6 weeks (longer if >150)**

PAI-1 Activity reference range should be 4.4 - 31 (reflex value is <4.4. - go to PAI-1 4G/5G genetic results at the end of this report) The reference range of >31.1 is looking for the PAI-1 deficiency, a bleeding disorder, not the overproduction of fibrin.

- **This is a measurement of how much plasminogen is being activated to make plasmin**
- **Reflexes to PAI-1 4G/5G genetic test if <4.4 (See genetic test information at end)**
- **95% of those with low activity come back with at least one copy of a PAI-1 4G deletion.**
- **Levels of PAI-1 inhibitor are not measured since we want to see functionally if there is sufficient activity.**
- **Those with low activity don't activate plasminogen well and therefore don't make enough plasmin to break down fibrin**

Protein S Activity (clottable) Published reference range of 63-140 is fine
Low Protein S causes extra production of fibrin and can result in increased clotting: https://pmc.ncbi.nlm.nih.gov/articles/PMC8373800/

- **This is a cofactor of Protein C and if low, indicates that there isn't enough vitamin K being synthesized by healthy gut lactobacilli.**
- **Low values are very common in patients who have been on long term or multiple courses of antibiotics. This is an acquired deficiency.**
- **If <65 treat with Vitamin K and butyrate (increases gut acidity so the probiotic will colonize) and oral Lactobacillus strains for two-months, then recheck Protein S. If normal they don't need those supplements anymore.**
- **If Protein S levels are significantly lower than reference range or they don't recover, order a Free Protein S Antigen to look for genetic Protein S deficiency.**
- **If they have a true Protein S Deficiency (genetic, not acquired) they will need to reduce the activation of Factor X with Apixaban dosed to normalize Prothrombin Fragments 1 + 2 lab values and prevent clotting events.**

Act. Prt C Resist w/FV Defic. (Activated Protein C Resistance w/Factor V Deficiency) – reflexes if <2.2 %
(LabCorp reference range of 2.2 to 3.5 is fine)

- **Screening test for Leiden Factor V. Positives will reflex to Leiden Factor V genetic test if resistance is low since APCR slows down Factor V. 100% of those with low APCR have a Leiden Factor V mutation. (See Leiden Factor V reflex information at end if reflexed.)**

Thrombin Antithrombin Complex (T/ATs) (LabCorp reference range of <4.3 is fine)

- **These are the body's healthy response when there has been a "thrombin burst" activated by injury such as a traumatic blood draw (multiple sticks or fishing for the vein). If high, be concerned that this was the cause and confirm by checking if Prothrombin Fragments 1 + 2 are also significantly elevated. LabCorp should repeat at no charge if both are extremely elevated.**
- **T/AT Complexes can also go up to block thrombin formation when body is making too much fibrin. If they are not increasing enough when fibrinogen or prothrombin fragments are high, they likely have a genetic reason (Factor II, V, or PAI-1 4G deletion).**
- **T/AT Complexes are considered good when the body can put the brakes on – fine to see in the teens, 20s, or 30's. If significantly higher (hundreds or thousands), the elevation is probably related to trauma).**

Factor II Gene Mutation Result G-G (Normal-Normal)

- **Any copies (heterozygous or homozygous) results in too much fibrin generation and are associated with an increased risk of clotting events (travel and post-operatively), cardiovascular disease, miscarriages, and chronic infections embedded in fibrin biofilms.**
- **This is a prothrombin G20210A mutation resulting in too much prothrombin production.**
- **The person will produce too much fibrin continuously (verified by measuring Prothrombin Fragments 1 + 2).**
- **If Prothrombin Fragments are elevated Apixaban 2.5 mg bid is needed to normalize fibrin production. Dosage can be adjusted as needed based on Prothrombin Fragment 1+2 labs – recheck periodically to find dosage that person needs to be "normalized."**
- **This will also reduce biofilm production and buildup of atherosclerotic plaque, but Boluoke is also needed to clear out what has accumulated previously.**

Prothrombin Fragment 1+2 MoAb LabCorp reference <326 < 310 pmol/L (preferred value)
Those with triggers for extra fibrin production (mycotoxins, high homocysteine, tick-borne infections, autoimmunity, etc.) weren't excluded from the reference range nor those with Factor II or V mutations who always generate too much fibrin.

- **This value correlates with the amount of fibrin being generated in real time. High levels are a concern due to the risk of a clotting event.**
- **If >350 this person is generating high levels of fibrin which is ending up in biofilms, contributing to atherosclerotic plaque, or setting them up for a clotting event. A clotting event is of particular concern if over 400.**
- **Lovenox at a prophylactic dose is used. 30 mg SC qd (subcutaneous injection every day) for 1 to 3 months. If they weigh >180 lb, 40 mg is dosed. This is a prophylactic, not an anti-coagulation dosage and will only normalize fibrin production, not anti-coagulate.**

- **Lovenox can quickly be reversed but we are normalizing their clotting, not anti-coagulating them. Preventing a clotting event is far more important than any imagined risk.**
- **Applying an ice pack to the injection site before and after the SC injection in the abdomen reduces bruising significantly.**
- **Lovenox has great anti-inflammatory properties but if the patient is unable to do injections, Apixaban 2.5 mg po bid will also block activation of Factor X and slow down fibrin production.**
- **Recheck prothrombin fragments 1 + 2 in a month. [Note: They are being normalized, not anti-coagulated.]**
- **You can generally manage with Boluoke once Prothrombin Fragments are <350.**
- **If they have Factor II or Leiden Factor V mutations, they will often need Apixaban for life, but if high fibrin production is due to other factors, dampening the activation of Factor X won't be needed once those triggers are treated.**

REFLEX TESTS

PAI-1 4G/5G Genetic Normal is 5G/5G. The deletion is reported as 4G/5G (heterozygous) or 4G/4G homozygous.

- **PAI-1 4G deletions are associated with an increased risk of clotting events (travel and post-operatively), cardiovascular disease, miscarriages, and chronic infections embedded in fibrin biofilms.**
- **This is NOT a variation or mutation, but a true deletion therefore, there is no significant difference functionally if heterozygous vs homozygous since both have low PAI-1 Activity.**
- **These individuals will need lumbrokinase the rest of their lives to break down the fibrin their body is making but not breaking down sufficiently. This is dosed at 2 capsules together once/day on an empty stomach, by itself, only water for 30 minutes afterwards.**
- **Pregnancies are managed with Lovenox although since miscarriages occur in the first 6 to 12 weeks, Boluoke has been found to be safe in early pregnancy and recommended until Lovenox can be initiated. ASA is not appropriate since it works on platelets, not fibrin.**

Leiden Factor V Genetic Any mutated copies (heterozygous or homozygous) result in too much fibrin generation.

- **The person will produce too much fibrin continuously (verified by measuring Prothrombin Fragments 1 + 2).**
- **If Prothrombin Fragments are elevated Apixaban 2.5 mg bid is needed to normalize fibrin production. Dosage can be adjusted as needed based on Prothrombin Fragment 1+2 values – recheck periodically to find dosage that person needs to be "normalized."**
- **This will also reduce biofilm production and buildup of atherosclerotic plaque, but Boluoke is also needed to clear out what has accumulated previously.**

Anyone with a genetic finding (elevated Lp(a), Factor II mutation, Leiden Factor V mutation, or PAI-1 4 G deletion) is in the 20% of the population with these genetics and will have the tendency to make biofilms contributing to chronic infections including long COVID, develop cardiovascular disease, and be at higher risk of clotting events. Elevated Lp(a) is more closely associated with pre-eclampsia but less miscarriages than the others. Blood relatives (parents, siblings, children after puberty) should also be screened for these factors and treated appropriately.