ALPHA-1 ANTITRYPSIN GENETIC TESTING in British Columbia

- Alpha 1 antitrypsin deficiency may be tested for by a number of algorithms. In BC, the disorder may be investigated by following the protocol advocated by Snyder et al¹ with some modifications. The protocol is summarized below and included in more detail on page 2:
- a) Initial test: Serum A1AT level stop here if A1AT level is > 1.15 g/L.
- b) Presumptive diagnostic test(s): stop here if diagnosis is clear.
 - PCR analysis (to detect "S" and "Z" alleles)
 - Isoelectric focusing (phenotype identification, if indicated)
- c) Definitive diagnostic test:
 - a) Gene sequencing to be performed when presumptive diagnostic test(s) yield ambiguous results.

To Test Your Patient:

1.Send your patient to the lab with:

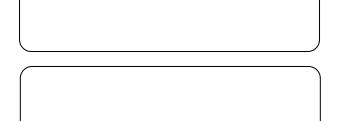
- a. a completed copy of the attached requisition with your patient
- b. If available, a copy of the hospital/lab serum level report (quantitative alpha-1 antitrypsin (AAT) level)

LABORATORIES WILL SHIP BOTH EDTA WHOLE BLOOD AND SERUM SAMPLES TO:

Dr. Andre Mattman Dept of Pathology & Laboratory Medicine St Paul's Hospital 1081 Burrard St., Vancouver, British Columbia, V6Z 1Y6

Alpha-1-Antitrypsin genetic testing in BC

Ship Samples c/o Dr. Andre Mattman Dept of Pathology & Laboratory Medicine St Paul's Hospital 1081 Burrard St., Vancouver, British Columbia, V6Z 1Y6



PATIENT NAME:	AGE:	BIRTHDATE:
MRN:	REFERRING PHYSICIAN	
ADDRESS OF REFERRING LABORATORY:	CONTACT TEL. NUMBER:	DATE & TIME OF COLLECTION :

CLINICAL HISTORY INCLUDES REFERRAL REQUEST AND HOSPITAL TELEPHONE NUMBERS

Reason for Testing		Lung Disease	Liver Disease
 Adult with clinical symptoms of A1AT deficiency* (investigation warranted for patients with a serum A1AT quantitative level < 1.15 g/L) 			
2. Neonate with cholestatic jaundice (send DNA extract, or whole blood, or NBS filter paper card)			
3. Asymptomatic patient – genetic testing for genetic counseling purposes only*			
IF previous investigations for A1AT deficiency have been done, list them below:	Date and Location of Test (include lab report if available)	Patient results	Normal Value for Iab
Serum A1AT quantitative level			g/L
Previous Genotyping or Phenotyping Result			N/A

ALPHA-1 ANTITRYPSIN (A1AT) GENETIC TESTING in British Columbia

		Patient Type		
Test Type	Test Method	Symptomatic Patient	1 st Degree Relative of Proband	Preconceptual Counseling
Initial Investigation	Serum A1AT Level	A1AT level determines need to proceed to Diagnostic test		
Preliminary Diagnostic:	PCR based DNA testing for S and Z mutations Protease inhibitor	Stop here if the preliminary diagnostic test result agrees with the serum A1AT level (see Table of Expected Values by Presumptive Genotype)		
	Isoelectric focusing (if indicated)			
Definitive Diagnostic	Gene Sequencing of coding region of the <i>SERPINA1</i> gene	Utilize to investigate cases in which the preliminary diagnostic test does not explain a relatively low serum A1AT level.		

Table of Expected Values by Presumptive Genotype¹

Genotype	mean	-1.28 SD (10th percentile)	+2 SD (97.5th percentile)
мм	1.47	0.91	2.35
MS	1.2	0.73	1.94
SS	0.88	0.65	1.24
MZ	0.85	0.59	1.25
SZ	0.6	NA	0.82
ZZ	0.28	N/A	0.72

References:

- 1. Snyder MR, Katzmann JA, Butz ML, et al. Diagnosis of alpha-1-antitrypsin deficiency: An algorithm of quantification, genotyping, and phenotyping. *Clin Chem.* 2006;52(12):2236-2242.
- Prins J, van der Meijden BB, Kraaijenhagen RJ, Wielders JP. Inherited chronic obstructive pulmonary disease: New selective-sequencing workup for alpha1-antitrypsin deficiency identifies 2 previously unidentified null alleles. *Clin Chem*. 2008;54(1):101-107.