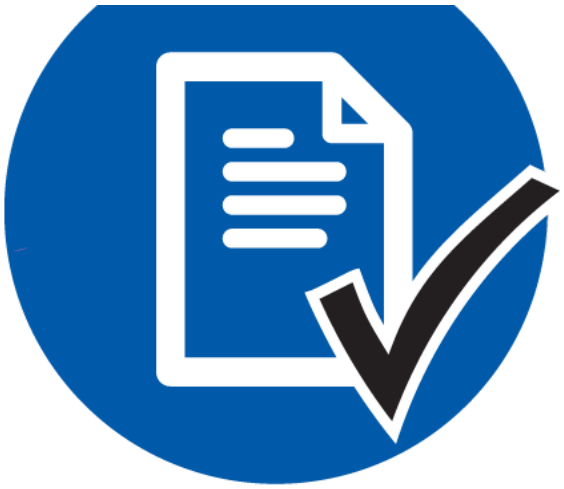
COLLEGE of AMERICAN PATHOLOGISTS

December 2024 Changes

Chemistry and Toxicology Checklist

CAP Accreditation Program



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Using the Changes Only Checklist

This document contains new checklist requirements, major and minor requirement revisions, and changes to explanatory text**. Changes appear in a track changes format that compares the previous checklist edition to the December 26, 2024.** Requirements with significant revisions will display a "Revised" flag. These changes may affect your laboratory operations. Requirements with minor revisions will not display a "Revised" flag. They are editorial changes that are not likely to affect your laboratory operations.

Information regarding requirements that are new or have been combined, moved, resequenced or deleted, as applicable, appears in table format below.

2024 CHECKLIST EDITION CHANGES
NEW, DELETED, MERGED, AND MOVED REQUIREMENTS *

2023 Requirement		Action Taken	2024 Requirement	
		New	CHM	12925
		New	CHM	15225
CHM	31100	Deleted		
		New	CHM	31150
CHM	31200	Merged	CHM	31150
CHM	31300	Merged	CHM	31150
CHM	31400	Merged	CHM	31150
CHM	31500	Merged	CHM	31150
CHM	31550	Merged	CHM	31150
CHM	31600	Merged	CHM	31150
CHM	31650	Merged	CHM	31150
CHM	31700	Merged	CHM	31150
CHM	32100	Merged	CHM	31150

*Deleted – Removed the requirement from the checklist edition
*Merged – Combined the requirement with a similar requirement in the same or different checklist
*Moved – Relocated the requirement to another checklist or resequenced it within the same checklist

ON-LINE CHECKLIST DOWNLOAD OPTIONS

Participants of the CAP accreditation programs may download the checklists ~~from the CAP website (cap.org)~~ by logging into cap.org and going to e-LAB Solutions Suite - Accreditation Checklists. They are available in different checklist types and formatting options, including:

- Master — contains ALL of the requirements and instructions available in PDF, Word/XML or Excel formats
- Custom — customized based on the laboratory's activity (test) menu; available in PDF, Word/XML or Excel formats
- Changes Only — contains only those requirements with significant changes since the previous checklist edition in a track changes format to show the differences; in PDF version only. Requirements that have been moved or merged appear in a table at the end of the file.

INTRODUCTION

This checklist is used in conjunction with the All Common and Laboratory General Checklists to inspect a chemistry laboratory section or department.

Certain requirements are different for waived versus nonwaived tests. Refer to the checklist headings and explanatory text to determine applicability based on test complexity. The current list of tests waived under CLIA may be found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm.

Policy/Procedure icon - The placement of this icon next to a checklist requirement indicates that a written policy or procedure is required to demonstrate compliance with the requirement. The icon is not intended to imply that a separate policy or procedure is required to address individual requirements. A single policy or procedure may cover multiple checklist requirements.

Laboratories not subject to US regulations: *Checklist requirements apply to all laboratories unless a specific disclaimer of exclusion is stated in the checklist. When the phrase "FDA-cleared/approved test (or assay)" is used within the checklist, it also applies to tests approved by an internationally recognized regulatory authority (eg, CE-marking).*

CHEMISTRY & TOXICOLOGY GENERAL ISSUES

PROFICIENCY TESTING

*****NEW** 12/26/2024***

CHM.12925 **Hemoglobin A1C Testing** **Phase I**

For laboratories that use accuracy-based proficiency testing (PT) for hemoglobin A1C, the laboratory evaluates its results based on acceptable performance criteria of +/- 6% from the target value, with appropriate corrective action taken for each unacceptable result.

NOTE: The CAP recommends use of accuracy-based PT products, when possible, to evaluate the accuracy of hemoglobin A1C results. Due to limitations in product stability, this may not be available for laboratories outside of the US.

The Centers for Medicare and Medicaid Services (CMS) have established acceptable performance criteria for hemoglobin A1C as a regulated analyte at +/- 8% from the target value. The CAP and all CAP-accepted PT providers must use the +/- 8% criteria in the formal grading of the PT for reporting non-waived results to the CMS. For laboratories participating in the CAP's accuracy-based PT program for hemoglobin A1C, the CAP will also evaluate their results against the target value using +/- 6% performance criteria. This is provided in the participant evaluation and participant summary report. Laboratories must review their performance against the +/- 6% criteria and perform corrective action for each unacceptable result.

Evidence of Compliance:

✓ Records of accuracy-based PT evaluation using the +/- 6% performance criteria

REFERENCES

1) Sacks DB, Arnold M, Bakris GL, et al. Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus. *Clin Chem*. 2023; 69(8):808-68.

QUALITY MANAGEMENT

RESULTS REPORTING

***NEW** 12/26/2024*

CHM.15225 **eGFR and LDL Cholesterol Calculated Test Results** **Phase I**

Clinicians have access to information regarding the equation used to calculate results for estimated glomerular filtration rates (eGFR) and low-density lipoprotein (LDL) cholesterol.

NOTE: Calculated results may differ based on which equation is used. This may limit clinical assessment of results and/or comparability of calculated results across laboratories, particularly when the source equation is not readily available to providers.

The information can be made available to clinicians using different approaches, such as on the patient report, test reference guide, or inclusion of the equation name in the test name.

Evidence of Compliance:
- ✓ Patient reports with information on the calculation used **OR**
- ✓ Test reference guide or other mechanism for providing calculation information

REFERENCES
1) Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. *N Engl J Med*. 2021; 385(19):1737-49.
2) Sampson M, Ling C, Sun Qian, et al. A New Equation for Calculation of Low-Density Cholesterol in Patient With Normolipidemia and/or Hypertriglyceridemia. *JAMA Cardiol*. 2020; 5(5):540-48.

METHODS, INSTRUMENT SYSTEMS, AND EQUIPMENT

Mass Spectrometry (MS)

CHM.18640 **Validation ~~and~~, Monitoring, and Annual Verification of MS Data Analysis Tools** **Phase II**

The laboratory validates data analysis tools used for compound identification and quantification when first installed and after any modifications, as applicable, and verifies performance at least annually.

NOTE: Data analysis tools may be used for various processes, such as integration of targeted and untargeted peaks, evaluating acceptability of calibration and control performance, stability of baseline, calculation of ion mass ratios, discrimination of positive and negative results, and assessing risk of carryover. Data analysis tools (eg, software or code-based rules, algorithms, machine learning) used for automated data analysis must be verified using defined acceptability criteria. Version control of custom data analysis tools is required. Reassessment of lower limit of quantification (LLOQ) and other decision points may be used to ensure that a shift has not occurred due to instrument performance or another factor impacting assay performance.

Customized data analysis tools, and modifications to that software, should be appropriately documented and records should allow for tracking to identify persons that have added or modified that software. The purpose of the computer program, the way it functions, and its interaction with other programs must be clearly stated. The level of detail should be adequate to support troubleshooting, system modifications, or additional programming.

Evidence of Compliance:
- ✓ Records of validation and revalidation after modifications **AND**
- ✓ Records of monitoring for changes to software update tools and other change impacting performance

REFERENCES
1) Vincente FB, Lin DC, Haymond S. Automation of chromatographic peak review and order to result data transfer in a clinical mass spectrometry laboratory. *Clin Chim Acta.* 2019;498(11):84-9.

Inductively Coupled Plasma – Mass Spectrometry (ICP/MS)

CHM.20600 Common Interferences Minimized **Phase II**

When appropriate, oxides and doubly-charged species are minimized.

NOTE: Oxides and doubly-charged species are common interferences in ICP/MS. Oxides of various elements may have overlapping signals with elements of the same mass, thus leading to false-positive findings. Special techniques such as high resolution ICP/MS, dynamic-reaction cell and collision-reaction cell processes may eliminate the concern for oxide interference. Elements with a second ionization potential greater than or equal to 15.8 eV (the ionization potential of argon) may be doubly-charged. Such doubly-charged species may suggest the presence of an element that is not truly present. For example, gadolinium has an isotope at m/e154. It has a doubly-charged species at m/e 77, which is also the same mass as an isotope of selenium~~, as well as a mass used as a correction factor for arsenic interference by $ArCl^{37}$. Despite the potential for a doubly-charged species, if the analyte of interest cannot be interfered with by known doubly-charged species, then such concern is unwarranted~~.

GENERAL CHEMISTRY

PRENATAL SCREENING

Requisitions/Calculations/Reports

Requests for prenatal screening (neural tube defects, Down syndrome, etc.) must include specific information for meaningful interpretation of laboratory tests. For clinical screening purposes, analyte concentrations must be converted to multiple of the median (MoM) values, using gestational-age specific medians. The MoM value is used directly as the interpretative result for neural tube defect screening and for calculating risk for fetal trisomies. Gestational age-specific MoM values need to be adjusted for each patient, based on several variables. The laboratory must work cooperatively with the clinician to ensure that all necessary information is obtained.

A listing of published references is available with CHM.31150 (Prenatal Screen Risk Calculation) in the Master version of the checklist available for download by logging into cap.org and going to e-LAB Solutions Suite - Accreditation Checklists.

~~**CHM.31100 Prenatal Screen Requisitions - Gestational Age**~~ **Merged with CHM.31150** ~~**Phase II**~~

~~**Prenatal screening requisitions require the first day of the last menstrual period (LMP), the estimated date of delivery or estimated gestational age by ultrasound dating.**~~

~~*NOTE: Accurate screening requires that the laboratory know the clinician's best estimate of the gestational age at the time of the specimen collection. The gestational age allows determination of the best optimal median values for a given screen.*~~

~~REFERENCES~~
~~1) Wald NJ, *et al*. Maternal serum-alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. Report of U.K. collaborative study on alpha-fetoprotein in relation to neural tube defects. *Lancet.* 1977;i:1323-1332.~~
~~2) Loughna, et al. Fetal size and dating: charts recommended for clinical obstetric practice. *Ultrasound.* 2009; 17.161-67.~~

3) ~~Wald NJ, et al. Prenatal screening for open neural tube defects and Down syndrome: Three decades of progress. *Prenat Diagn.* 2010; 30:519-21.~~
4) ~~Ioannou C, et al. Standardization of crown-rump length measurement. *BJOG.* 2013; 2(suppl):38-41.~~

***NEW** 12/26/2024*

CHM.31150 Prenatal Screen Risk Calculation Phase II

The laboratory determines which information and adjustments to include in the prenatal screening risk calculation.

NOTE: Expected elements in the prenatal risk calculation include:

- *Gestational age*
- *In vitro fertilization method, if applicable*
- *Initial or repeat testing*
- *Maternal age*
- *Maternal race or subpopulation as defined by the laboratory*
- *Maternal weight*
- *Medications to control diabetes*
- *Multiple gestation, if applicable*
- *Smoking status*

The rationale for exclusion of any expected element must be documented. Additional elements may be included in calculating the risk categorization. The rationale for additional elements must be documented.

REFERENCES

1) Wald NJ, *et al*. Maternal serum-alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. Report of U.K. collaborative study on alpha-fetoprotein in relation to neural tube defects. *Lancet.* 1977;i:1323-1332.
2) Loughna, et al. Fetal size and dating: charts recommended for clinical obstetric practice. *Ultrasound.* 2009; 17.161-67.
3) Wald NJ, et al. Prenatal screening for open neural tube defects and Down syndrome: Three decades of progress. *Prenat Diagn.* 2010; 30:519-21.
4) Ioannou C, et al. Standardization of crown-rump length measurement. *BJOG.* 2013; 2(suppl):38-41.
5) Cuckle HS, *et al*. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. Brit J Obstet Gynecol. 1987; 94:387-402.
6) Morris JK, Wald NJ. Estimating the risk of Down syndrome in antenatal screening and the gestation at which this applies. J Med Screen. 2008; 14(1):5-7.
7) Haddow JE, Palomaki GE, Canick JA, Knight GJ. Prenatal screening for open neural tube defects and Down's syndrome. In: Rodeck CH, Whittle MJ, ed. *Fetal Medicine: Basic Science and Clinical Practice.* 2nd ed. Churchill Livingstone: London;2009:243-264.
8) Watt HC, Wald NJ, Smith D, Kennard A, Densem J. Effect of allowing for ethnic group in prenatal screening for Down's syndrome. *Prenat Diagn.* 1996;16(8):691-8.
9) Benn PA, Clive JM, Collins R. Medians for second-trimester maternal serum alpha-fetoprotein human chorionic gonadotrophin, and unconjugated estriol; differences between races or ethnic groups. *Clin Chem* 1997 43(2):333-7
10) Cowans NJ, Spencer K. Effect of gestational age on first trimester maternal serum prenatal screening corrections for ethnicity and IVF conception. *Prenat Diagn.* 2013; 33(1):56-60.
11) Ball S, et al. Temporal effects of maternal and pregnancy characteristics on serum pregnancy-associated plasma protein-A and free beta human chorionic gonadotrophin at 7-14 weeks gestation. *Ultrasound Obstet Gynecol.* 2013; 41(1):33-9.
12) Burns NR, Kolarova T, Katz R, Ma K, Delaney S. Reconsidering race adjustment in prenatal alpha-fetoprotein screening. *Obstet Gynecol.* 2023; 141:438-44.
13) Haddow JE, Kloza EM, Knight GJ, Smith DE. Relation between maternal weight and serum alpha-fetoprotein concentration during the second trimester. *Clin Chem.* 1981; 27(1):133-4.
14) Neveux LM, *et al.* Refinements in managing maternal weight adjustment for interpreting prenatal screening results. *Prenat Diag.* 1996;16:1115-1119
15) Wright D, Papadopoulos S, Silva M, Wright A, Nicolaides KH. Serum free β-human chorionic gonadotrophin in the three trimesters of pregnancy: effects of maternal characteristic's and medical history. *Ultrasound Obstet Gynecol.* 2015; 46(1):51-9.
16) Wright D, Papadopoulos S, Silva M, Wright A, Nicolaides KH. Serum pregnancy-associated plasma protein-A in the three trimesters of pregnancy: effects of maternal characteristic's and medical history. *Ultrasound Obstet Gynecol.* 2015; 46(1):42-50.
17) Wald NJ, *et al.* Maternal serum alpha-fetoprotein and diabetes mellitus. *Br J Obstet Gynecol.* 1979;86:101-105
18) Sancken U, Bartels I. Biochemical screening for chromosomal disorders and neural tube defects (NTD): is adjustment of maternal alpha-fetoprotein (AFP) still appropriate in insulin-dependent diabetes mellitus (IDDM)? *Prenat Diagn*. 2001;21(5):383-6.
19) Hutley W, *et al.* Second-trimester prenatal screening markers for Down syndrome in women with insulin-dependent diabetes mellitus. *Prenat Diagn* 2004;24:804-807
20) Savvidou MD, Syngelaki A, Muhaisen M, Emelyanenko E, Nicolaides K. First trimester maternal serum free- β human chorionic gonadotrophin and pregnancy-associated plasma protein-A in pregnancies complicated by diabetes mellitus. *BJOG*. 2012;119:410-6.
21) Spencer K, Cowans NJ. The association between gestational diabetes mellitus and first trimester aneuploidy screening markers. *Ann Clin Biochem.* 2013; 50 (Pt 6):603-10.
22) Gurram P, Benn P, Campbell WA. Impact of diabetes on aneuploidy screening. *Clin Lab Med.* 2013;33(2):271-80.
23) Palomaki GE, Knight GJ, Haddow JE. Human chorionic gonadotropin and unconjugated estriol measurements in insulin-dependent diabetic pregnant women being screening for fetal Down syndrome. *Prenat Diagn.* 1994;14(1):66-8.
24) Ribbert LS, Kornman LH, De Wolf BT, et al. Maternal serum screening for fetal Down syndrome in IVF pregnancies.*Prenat Diagn*. 1996:16(1):35-8

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26) Canick JA, Hogan JW, Hackett RJ, Kellner LH, Saller DN Jr, Frishman GN, Serum triple-marker screening in in vitro fertilization and naturally conceived pregnancies.*Obstet Gynecol*. 1997 Jul:90(1):98-101.
27) Liao AW, Heath V, Kametas N, Spencer K, Nicolaides KH. First-trimester screening for trisomy 21 in singleton pregnancies achieved by assisted reproduction. *Hum Reprod*. 2001 Jul:16(7):1501-4.
28) Lambert-Messerlian G, Palomaki GE, Canick JA. Adjustment of serum markers in first trimester screening. *J Med Screen*. 2009;16(2):102-3.
29) Gjerris AC, Loft A, Pinborg A, Christiansen M, Tabor A.. First-trimester screening markers are altered in pregnancies conceived after IVF/ICSI. *Ultrasound Obstet Gynecol.* 2009 Jan;33(1):8-17.
30) Lanes A, Huang T, Sprague AE , Leader A, Potter B, Walker M. Maternal serum screening markers and nuchal translucency measurements in in vitro fertilization pregnancies: a systematic review. *Fertil Steril.* 2016 Nov;106(6):1463-1469.
31) Wald NJ, Rish S, Hackshaw AK. Combining nuchal translucency and serum markers in antenatal screening for Down's syndrome in twin pregnancies. *Prenat Diag.* 2003; 23(7):588-592.
32) Wald NJ, Rish S. Prenatal screening for Down syndrome and neural tube defects in twin pregnancies. *Prenat Diagn.* 2005;25:740-745
33) Madsen HN, et al. A reassessment of biochemical markers distributions in trisomy 21 affected and unaffected twin pregnancies in the first trimester. *Ultrasound Obstet Gynecol.* 2011; 37(1):38-47.
34) Hafner E, et al. Influence of cigarette-smoking on the result of the triple test. *Gynecol Obstet Invest.* 1999;47(3):188-90.
35) Huttly W, Bestwick J, Wald N. Effect of smoking status on inhibin-A in second-trimester prenatal screening for Down syndrome. *Prenat Diagn.* 2014;34(4):406-7.
36) Lambert-Messerlian G, Palomaki GE. Prenatal serum screening markers may not require adjustment in former smokers. *Prenat Diagn.* 2015;35(13):1371-3.
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38) Spencer K, et al. The impact of correcting for smoking status when screening for chromosomal abnormalities using maternal serum biochemistry and fetal nuchal translucency thickness in the first trimester of pregnancy. *Prenat Diag.* 2004;24(3):169-73.
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40) Zhang J, et al. Impact of smoking on maternal serum markers and prenatal screening in the first and second trimesters. *Prenat Diag.* 2011;31(6):583-8.
41) Estimating an individual's risk of having a fetus with open spina bifida and the value of repeat alphafetoprotein testing. Fourth report of the U.K. collaborative study on alphafetoprotein in relation to neural tube defects. *J Epidemiol Commun Health.* 1982;36:87-95
42) Cuckle HS, *et al.* Repeat maternal serum testing in multiple marker Downs syndrome screening programmes. *Prenat Diagn.* 1994;14:603-607
43) Hackshaw AK, *et al.* Repeat testing in antenatal screening for Down syndrome using dimeric inhibin-A in combination with other maternal serum markers. Prenat Diagn, 2001;21:58-61
44) Haddow JE, Palomaki GE, Knight GJ, Foster DL, Neveux LM. Second trimester screening for Down's syndrome using maternal serum dimeric inhibin A. *J Med Screen* 1998;5(3):115-9
45) Cuckle HS, Holding S, Jones R, Groome NP, Wallace EM. Combining inhibin A with existing second-trimester markers in maternal serum screening for Down's syndrome. *Prenat Diagn* 1996 16(12):1095-1100
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47) Messerlian G, Strickland SW, Wilbur J, et al. Use of maternal race and weight provides equitable performance in serum screening for open neural tube defects. *Clin Chem*. 2024; 70(7):948-56.

~~CHM.31200~~ ~~Prenatal Screen Requisitions - Maternal Birth Date~~ Merged with CHM.31150 ~~Phase II~~

~~**Prenatal screening requisitions require maternal birth date.**~~

~~*NOTE: Maternal age is needed to calculate the patient-specific risk for Down syndrome, however, is not necessary when screening for neural tube defects. The patient-specific risk, not the analyte concentration, is used as the screening variable to identify pregnancies at high-risk for Down syndrome. Maternal age is also a useful patient identifier.*~~

~~REFERENCES~~

~~1) Cuckle HS, *et al*. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. *Brit J Obstet Gynecol*. 1987;94:387-402~~
~~2) Morris JK, Wald NJ. Estimating the risk of Down syndrome in antenatal screening and the gestation at which this applies. *J Med Screen*. 2008; 14(1):5-7.~~
~~3) Haddow JE, Palomaki GE, Canick JA, Knight GJ. Prenatal screening for open neural tube defects and Down's syndrome. In: Rodeck CH, Whittle MJ, ed. *Fetal Medicine: Basic Science and Clinical Practice*. 2nd ed. Churchill Livingstone: London;2009:243-264.~~

~~CHM.31300~~ ~~Prenatal Screen Requisitions - Patient Race~~ Merged with CHM.31150 ~~Phase II~~

~~**Prenatal screening requisitions require patient race.**~~

~~*NOTE: PAPP-A values are approximately 25% higher in black women. AFP and hCG values in black women are approximately 10% to 15% higher than in Caucasian women, and DIA values in black women are approximately 8% lower than in Caucasian women. Adjustment is*~~

recommended for Down syndrome, and more importantly for trisomy 18 screening. The uE3 levels are similar in the two racial groups; uE3 medians need not be adjusted.

Depending upon the racial distribution of the patient population, the laboratory should either have separate marker medians for black women if enough data is available and Caucasian women, or apply an appropriate correction factor for patients from the less common races. Black women also have a lower birth prevalence of neural tube defects, and some screening programs raise the MoM cut-off to take this difference into account (after adjusting the AFP MoM value).

Current data indicate that statistically significant differences in median values exist for other races and ethnic groups (eg, Hispanic, Asian, Native American). Most differences tend to be small and do not materially affect the risk calculations for Down syndrome and neural tube defects. However, laboratories that screen large numbers of women may consider using median values specific to ethnic or racial groups if significant differences are identified in their screening population.

Written procedures should identify the decision-making process to include or not include adjustments of medians for race. If adjustments are made when screening women, the definition used to identify appropriate women and the adjustments factor for each analyte should be included in laboratory procedure.

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2) Benn PA, Clive JM, Collins R. Medians for second-trimester maternal serum alpha-fetoprotein human chorionic gonadotrophin, and unconjugated estriol; differences between races or ethnic groups. *Clin Chem* 1997 43(2):333-7
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4) Ball S, et al. Temporal effects of maternal and pregnancy characteristics on serum pregnancy-associated plasma protein-A and free beta human chorionic gonadotrophin at 7-14 weeks gestation. *Ultrasound Obstet Gynecol.* 2013; 41(1):33-9.

CHM.31400 Prenatal Screen Requisitions - Maternal Weight Merged with CHM.31150 Phase II

Prenatal screening requisitions require maternal weight.

NOTE: The concentration of all first trimester and second trimester markers decreases with increasing maternal weight. All first and second trimester markers must be adjusted for maternal weight. Heavier women have lower analyte values, and lighter women have higher levels. This is presumably due to a greater maternal blood volume in the former group. The influence of weight adjustment on neural tube defects screening is small, but adjustment aids in equalizing false positive and false negative rates in all weight categories. The linear-reciprocal equation model allows the correction equation to apply to a broader range of maternal weights than the log-linear model and only requires approximately 1000 data points per serum marker for calculation.

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CHM.31500 Prenatal Screen Requisitions - Medications to Control Diabetes Merged with CHM.31150 Phase II

Prenatal screening requisitions require a history of the patient receiving medication (eg, insulin) to control diabetes at the time of conception.

NOTE: In 1979, AFP levels in women who require insulin during pregnancy (but not before pregnancy) were reported and confirmed by others to be as much as 40% lower than in the general pregnancy population. This had important implications for open neural tube defect screening as pregnancies in women with insulin dependent diabetes mellitus (IDDM) were at a 5 to 10 fold higher risk of having an affected fetus. These observations were extended to the other serum markers, usually with smaller effects identified. The terminology, management and care of diabetes and related disorders during pregnancy have changed substantially over time. The majority of more recent studies find little or no effect of gestational diabetes requiring insulin or oral agents during pregnancy on any of the serum markers, including AFP. For these reasons, directors can individually determine whether adjustments in serum markers should be made for IDDM in their screened population and whether a different AFP screening cut-off should be used for open neural tube defect screening.

The written procedures should identify the decision-making process to include or not include adjustment for insulin dependent diabetes. If adjustments are made when screening women, the definition used to identify appropriate women and the adjustments factor for each analyte should be included.

REFERENCES

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7) Palomaki GE, Knight GJ, Haddow JE. Human chorionic gonadotropin and unconjugated estriol measurements in insulin-dependent diabetic pregnant women being screening for fetal Down syndrome. *Prenat Diagn.* 1994;14(1):66-8.

CHM.31550 Prenatal Screen Requisitions - In Vitro Fertilization Merged with CHM.31150 Phase I

Prenatal screening requisitions require a history of the patient's current in vitro fertilization status.

NOTE: There is sufficient evidence to suggest that screening pregnancy marker levels are influenced by in vitro fertilization methods. However, different IVF treatment methods and personal medical history seem to alter the screening parameters in different ways.

The written procedures should identify the decision-making process to include or not include adjustments for in vitro fertilization pregnancies. If adjustments are made when screening IVF pregnancies, the definition used to identify appropriate women and the adjustment factor for each analyte should be included in laboratory procedure.

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4) Hum Reprod. 2001 Jul;16(7):1501-4. First-trimester screening for trisomy 21 in singleton pregnancies achieved by assisted reproduction. Liao AW(1), Heath V, Kametas N, Spencer K, Nicolaides KH.
5) J Med Screen. 2009;16(2):102-3. Adjustment of serum markers in first trimester screening. Lambert-Messerlian G(1), Palomaki GE, Canick JA.
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7) Fertil Steril. 2016 Nov;106(6):1463-1469. Maternal serum screening markers and nuchal translucency measurements in in vitro fertilization pregnancies: a systematic review. Lanes A, Huang T, Sprague AE , Leader A, Potter B, Walker M.

~~CHM.31600~~ **~~Prenatal Screen Requisitions - Multiple Gestations~~** **Merged with CHM.31150** **~~Phase II~~**

~~Prenatal screening requisitions require clinical evidence of multiple gestations (twins, etc.).~~

~~NOTE: Women with ultrasonographically confirmed twin pregnancies have, on average, twice the level of AFP than that seen in women with singleton pregnancies at the same gestational age. Most laboratories use a screening cutoff level for twin pregnancies between 3.5 and 5.0 MoM, or divide the MoM by two and use an adjusted cutoff level as for singleton pregnancies. However, screening for neural tube defects in twin pregnancies is less efficient than singleton pregnancies. Approximately 50% of twin pregnancies with an open neural tube defect and 5% of unaffected twin pregnancies have a MoM of 4.5 or greater. If twin pregnancies are to be screened for Down syndrome, laboratories need to calculate risks using a method specifically designed for this application. PAPP-A, hCG, and dimeric inhibin A levels are also approximately twice as high in twin pregnancies, while uE3 levels in twin pregnancies are approximately 1.7 times as high as in singleton pregnancies. There are few data on analyte concentrations from twin pregnancies with one or both fetuses affected with Down's syndrome; therefore, only "pseudo risks" can be calculated. Pseudo risks are less reliable than those calculated for singleton pregnancy and some laboratories choose not to report the actual risk, but only report specimens as screen negative or screen positive. Insufficient data are available to calculate Down syndrome risk in pregnancies with three or more fetuses.~~

~~The written procedures should identify the decision-making process to include or not include adjustment for multiple gestations. If adjustments are made when screening women, the definition used to identify appropriate women and the adjustments factor for each analyte should be included.~~

~~REFERENCES~~

~~1) Wald NJ, Rish S, Hackshaw AK. Combining nuchal translucency and serum markers in antenatal screening for Down's syndrome in twin pregnancies. *Prenat Diag.* 2003; 23(7):588-592.~~
~~2) Wald NJ, Rish S. Prenatal screening for Down syndrome and neural tube defects in twin pregnancies. *Prenat Diagn. 2005;25:740-745*~~
~~3) Lambert-Messerlian G, Palomaki GE, Canick JA. Adjustment of serum markers in first trimester screening. *J Med Screen.* 2009; 16(2):102-3.~~
~~4) Madsen HN, et al. A reassessment of biochemical markers distributions in trisomy 21 affected and unaffected twin pregnancies in the first trimester. *Ultrasound Obstet Gynecol.* 2011; 37(1):38-47.~~

~~CHM.31650~~ **~~Prenatal Screen Requisition - Cigarette Smoking Status~~** **Merged with CHM.31150** **~~Phase I~~**

~~Prenatal screening requisitions require a history of the patient's current cigarette smoking status.~~

~~NOTE: Cigarette smoking has a well-described and important impact on several of the markers used in prenatal screening. The largest effects are seen for second trimester hCG and inhibin-A measurements. In the first trimester, both free beta hCG and hCG as well as PAPP-A are also influenced. The use of multiple markers tends to reduce the overall impact on risk (eg, lower hCG in smokers tends to reduce risk, while higher inhibin-A in smokers tends to increase risk). A simple question (Do you currently smoke cigarettes?) is reliable; the numbers smoked per day is less important. Gaps in knowledge include effect of vaping, recent smoking cessation and cigar smoking where inhaling is less common. There appears to be no or minimal effect of maternal smoking on the birth prevalence of Down syndrome. Given the important changes and the attempt to individualize risk estimates, laboratory directors should examine how smoking could be incorporated into their screening program and record their decision on whether their programs routinely account for smoking status. Written procedures should identify the decision-making process to include or not include adjustment for cigarette smoking. If adjustments are made when screening women, the definition used to identify appropriate women and the adjustments factor for each analyte should be included in laboratory procedure.~~

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1) Hafner E, et al. Influence of cigarette-smoking on the result of the triple test. *Gynecol Obstet Invest.* 1999;47(3):188-90.
2) Huttly W, Bestwick J, Wald N. Effect of smoking status on inhibin-A in second-trimester prenatal screening for Down syndrome. *Prenat Diagn.* 2014;34(4):406-7.
3) Lambert-Messerlian G, Palomaki GE. Prenatal serum screening markers may not require adjustment in former smokers. *Prenat Diagn.* 2015;35(13):1371-3.
4) Palomaki GE, et al. Cigarette smoking and levels of maternal serum alpha-fetoprotein, unconjugated estriol, and hCG: Impact on Down syndrome screening. *Obstet Gynecol.* 1993;81(5):675-8.
5) Spencer K, et al. The impact of correcting for smoking status when screening for chromosomal abnormalities using maternal serum biochemistry and fetal nuchal translucency thickness in the first trimester of pregnancy. *Prenat Diag.* 2004;24(3):169-73.
6) Rudnicka AR, et al. Influence of maternal smoking on the birth prevalence of Down syndrome and on second trimester screening performance. *Prenat. Diagn.* 2002;22(10):893-7.
7) Zhang J, et al. Impact of smoking on maternal serum markers and prenatal screening in the first and second trimesters. *Prenat Diag.* 2011;31(6):583-8.

CHM.31700 **Prenatal Screen Requisitions - Initial/Repeat Testing** **Merged with CHM.31150** **Phase I**

Prenatal screening requisitions require information on whether the testing is being performed for initial screening for a given test or as a repeat sample for the same test.

NOTE: The interpretation of a repeat maternal serum sample may be different from the interpretation of an initial serum specimen. In neural tube defect screening using AFP, a repeat sample can be interpreted as if it were an initial sample if fixed MoM cut-offs are used to identify high-risk women. If patient-specific risks are calculated for a repeat test result, one should combine the results of both the initial and repeat sample, using published algorithms. Repeat testing is not recommended for Down syndrome screening unless a sample is drawn too early for reliable interpretation. If a test on a second sample is performed, it is essential that the revised risk be calculated using the results from both samples. A method has been published for these calculations.

REFERENCES
1) Estimating an individual's risk of having a fetus with open spina bifida and the value of repeat alphafetoprotein testing. Fourth report of the U.K. collaborative study on alphafetoprotein in relation to neural tube defects. *J Epidemiol Commun Health.* 1982;36:87-95
2) Cuckle HS, *et al.* Repeat maternal serum testing in multiple marker Downs syndrome screening programmes. *Prenat Diagn.* 1994;14:603-607
3) Hackshaw AK, *et al.* Repeat testing in antenatal screening for Down syndrome using dimeric inhibin-A in combination with other maternal serum markers. Prenat Diagn, 2001;21:58-61

CHM.31900 **Median Value ReverificationReview** **Phase II**

Medians are reverifiedreviewed at specified intervals or test volumes and when new reagent lots are introduced, and the medians are recalculated if necessary.

NOTE: Systematic shifts in analyte values observed with new reagent lots can cause significant deterioration in screening performance if not taken into account. One method for assessing a new lot is performing a split specimen comparison study between the new and old lot typically using 25 to 50 specimens. Bias between an existing and a new lot, if important (eg,>5%) can then be taken into account by adjusting the existing set of median values (or median equation).

In addition, re-evaluationreview of medians at specified intervals is a valuable quality control mechanism to ensure validity of reported MoMs. Epidemiological monitoring of Down syndrome screening can be accomplished by determining the median MoM value at frequent intervals (eg, every 500-1000 patients, or weekly or monthly). If a persistent shift is noted (median MoM less than 0.90 or greater than 1.10)),), new medians should be determined. Records of the median MoMs must be retained.

Evidence of Compliance:

✓ Records of median value recalculation or reverification datacalculation or review at defined frequency or test volume

REFERENCES
1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda, Maryland. The quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural tube defects. *Clin Chim Acta.* 1980;105:9-24
2) Erickson JA, Ashwood ER, Gin CA. Evaluation of a dimeric inhibin-A assay for assessing fetal Down syndrome: establishment, comparison, and monitoring of median concentrations for normal pregnancies. *Arch Pathol Lab Med,* 2004 Apr;128(4):415-20.
3) Ashwood ER, Grenache DG, Lambert-Messerlian G. Pregnancy and its Disorders. *In: Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed.* Burtis CA, Ashwood ER, Bruns DE (eds), Elsevier Saunders: Philadelphia, PA, 2011.

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CHM.31950 ~~Establishing~~ Nuchal Translucency (NT) ~~Measurements~~Measurement Quality **Phase I**

If screening panels are offered using nuchal translucency (NT) values, the laboratory has ~~criteria for their establishment and use.~~

NOTE: The NT value is an important component of the test and may impact the results. Risk assessment can be used to determine if laboratories report the NT results.

~~*Potential criteria include:*~~

- ~~*Requirements for verifying the credentialing of each sonographer*~~
- ~~*Having sonographers provide a set number of NT/CRL measurements prior to initial interpretations*~~
- ~~*Implementing sonographer-specific medians when the median NT MoM levels are outside of set limits*~~
- ~~*Reviewing data for sonographers available from certifying organization (eg, NT Quality Review Program - NTQR (https://ntqr.perinatalquality.org) or the Fetal Medicine Foundation - FMF (http://fetalmedicineusa.com)*~~
- ~~*Establishing communication with sonographers to inform them of monitoring results*~~
- ~~*Establishing communications with credentialing organizations to inform them of sonographer performance*~~

Evidence of Compliance:

- ~~✓ Records of sonographer establishment~~
- ✓ Documentation of a quality assurance process

REFERENCES
1) American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No 77: Screening for fetal chromosomal abnormalities. *Obstet Gynecol.* 2007;109:217-27.
2) Ashwood ER, Grenache DG, Lambert-Messerlian G. Pregnancy and its Disorders. *In: Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed.* Burtis CA, Ashwood ER, Bruns DE (eds), Elsevier Saunders: Philadelphia, PA, 2011.
3) Schuchter K, et al. The first trimester 'combined test' for the detection of Down syndrome pregnancies in 4939 unselected pregnancies. *Prenat Diagn.* 2002; 22(3):211-5.
4) Malone FD, et al. Use of overall population, center-specific, and sonographer-specific nuchal translucency medians in Down Syndrome screening: which is best? (results from the faster trial). *Am J Obstet Gynecol.* 2003; 189(6):S232.
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6) Malone FD, D'Alton ME. First trimester sonographic screening for Down syndrome. *Obstet Gynecol.* 2003; 102(5):1066-79.

CHM.31960 ~~Reverification~~Monitoring of Nuchal Translucency (NT) Measurements **Phase I**

If screening panels are offered using nuchal translucency (NT) values, the laboratory routinely performs epidemiological monitoring of these measurements.

NOTE: An example of such a monitoring procedure (with action limits) is provided below. For each sonographer with sufficient data (typically at least 30 to 50 measurements over six months), monitor and provide limits for three quality parameters.

- *Percent increase in NT measurements (in mm) by gestational age (eg, 15% to 35%)*
- *The NT median MoM (eg, 0.90 to 1.10) or the delta NT (eg, ±0.05 mm)*
- *The distribution of NT MoMs after a logarithmic transformation (log standard deviation), (eg, 0.08 to 0.13)*

Evidence of Compliance:

✓ Records of NT median data study(ies) **AND**

✓ Records of review at defined frequency

REFERENCES

1) Palomaki GE, Neveux LM, Donnenfeld A, Lee JE, McDowell G, Canick JA, Summers A, Lambert-Messerlian G, Kellner LH, Zebelman A, Haddow JE. Quality assessment of routine nuchal translucency measurements: A North American laboratory perspective. *Genet Med*, 2008 Feb;10(2):131-8
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3) Palomaki GE, *et al.* Technical standards and guidelines: Prenatal screening for Down syndrome that includes first-trimester biochemistry and/or ultrasound measurements. *Genet Med,* 2009;11(9):669-681
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~~**CHM.32100 Screening Panel Marker Addition** **Merged with CHM.31150** **Phase II**~~

~~**If the laboratory adds another marker to its screening panel, it follows the same requirements outlined for established markers.**~~

~~*NOTE: The laboratory must demonstrate that it adheres to the checklist items outlined for established markers in the Prenatal Screening section. These include establishing median values appropriate for the population being screened, and adjusting where appropriate for variables that have been shown to influence analyte values, such as maternal weight, maternal race, insulin dependent diabetes, smoking, and twin pregnancy. Laboratories must verify that the risks calculated using the additional marker are valid.*~~

~~**Evidence of Compliance:**~~

~~✓ Records of validation studies of other markers added to the screening panel~~

~~REFERENCES~~

~~1) Haddow JE, Palomaki GE, Knight GJ, Foster DL, Neveux LM. Second trimester screening for Down's syndrome using maternal serum dimeric inhibin A. J Med Screen 1998;5(3):115-9~~
~~2) Cuckle HS, Holding S, Jones R, Groome NP, Wallace EM. Combining inhibin A with existing second-trimester markers in maternal serum screening for Down's syndrome. *Prenat Diagn* 1996 16(12):1095-1100~~
~~3) Clinical and Laboratory Standards Institute. Maternal Serum Screening; *Approved Guideline.* 2nd ed. CLSI Document I/LA25-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2011.~~

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CHM.32300 Prenatal Screen ~~Reports~~Requisition and Report **Phase II**

The prenatal screen requisition and report ~~contains~~contain all information collected from the provider that is relevant to the clinical interpretation of the results.

~~*NOTE: Not all relevant information is provided for every woman screened and the laboratory director may choose to not provide a clinical interpretation if critical information is missing (eg, gestational age, maternal age). In order, with the most critical information first, this would include:*~~

- ~~*Estimate of gestation age based preferably on an ultrasound examination*~~
- ~~*The woman's date of birth or estimated age at delivery*~~
- ~~*Singleton or multiple gestation*~~
- ~~*Maternal weight*~~
- ~~*Maternal race*~~
- ~~*Family history of neural tube defects or common aneuploidies*~~
- ~~*Cigarette smoking status*~~
- ~~*Maternal insulin dependent diabetic prior to pregnancy*~~
- ~~*Initial or repeat test request*~~
- ~~*Information on in vitro fertilization*~~

NOTE: Prenatal screen risk calculation requisitions must include the information required by the laboratory to perform the risk assessment.

Evidence of Compliance:
- ✓ Requisitions with required elements **AND**
- ✓ Reports with required elements

CHM.32400 Multiple of Population Median **Phase II**

Test results are reported as multiples of the population median (MoM).

NOTE: Reporting of results in terms of multiple of the population median (MoM) simplifies interpretation at various gestational ages, reduces possible systematic between-laboratory and between-kit bias in assay results, and facilitates comparison among laboratories. Laboratories can also compare their experiences with large-scale published studies more readily by using MoM as the reportable interpretive unit. The initial MoM is calculated as the measured analyte value divided by the median value for the appropriate gestational age. The MoM should also be adjusted for the other clinical variables known to influence the concentration of each analyte, generally by dividing by a factor specific for each variable. ~~Such clinical variables that may require correction factors include race, weight, smoking, twin, IDDM status, and repeat testing in same pregnancy.~~

REFERENCES
1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda Maryland. The quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural tube defects. *Clin Chim Acta.* 1980;105:9-24
2) Clinical and Laboratory Standards Institute (CLSI). *Maternal Serum Screening; Approved ~~Guideline—~~Standard - Second Edition.* CLSI document I/LA25-A2 ~~(ISBN 1-56238-749-9). CLSI, 940 West Valley Road, Suite 1400~~, Clinical and Laboratory Standards Institute, Wayne, ~~Pennsylvania 19087-1898 USA,~~PA; 2011.

Amniotic Fluid Alpha-fetoprotein (AFAFP)

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CHM.32800 Median Value ~~Reverification~~Calculation and Review **Phase II**

AFAFP medians are ~~recalculated or reverified~~calculated and reviewed at specified intervals.

Evidence of Compliance:
- ✓ Records of median values ~~recalculation or reverification~~calculation and review at defined frequency

CHM.32900 Multiple of Median **Phase II**

AFAFP results are reported in multiples of the median (MoM).

NOTE: Reporting of AFAFP results in terms of multiples of the median (MoM) simplifies interpretation at various gestational weeks, reduces the systematic between-laboratory and between-kit bias in results, and facilitates comparison of results between laboratories. Laboratories may compare their experiences with large-scale published studies much more readily when using MoM as the interpretive unit for AFP measurements. ~~AFAFP concentrations are higher in black women than in whites and may be different in other racial groups as well. Although no simple correction factors are available at present, the use of race-specific medians is worth consideration.~~

REFERENCES
1) Wald NJ, *et al.* Amniotic fluid acetylcholinesterase measurement in the prenatal diagnosis of open neural tube defects. *Prenat Diagn.* 1989;9:813-829
2) Clinical and Laboratory Standards Institute (CLSI). *Maternal Serum Screening; Approved Guideline—Second Edition*. CLSI document I/LA25-A2 (ISBN 1-56238-749-9). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2011

HIV PRIMARY DIAGNOSTIC TESTING

CHM.33790 HIV Primary Diagnostic Testing - Supplemental and Confirmatory Testing Phase I

The laboratory follows public health recommendations or guidelines for HIV primary diagnostic testing, including primary screening and additional (supplemental and/or confirmatory) testing.

NOTE: If additional testing after a primary screening test is recommended by public health authorities, the laboratory:

- *Performs additional testing reflexively if the specimen is suitable and the test is performed in house, or*
- *Sends additional testing to a referral laboratory if the specimen is suitable, or*
- *Provides guidance to providers on submission of additional specimens, if needed for supplemental or confirmatory testing.*

The US Centers for Disease Control and Prevention (CDC) and Association of Public Health Laboratories (APHL) provide recommendations for HIV testing. Guidelines and recommended algorithms can be found on the CDC and APHL websites.

~~*This checklist item does not apply to the testing of individuals from whom human derived products for therapeutic use are being derived or other types of testing performed for the monitoring of HIV infection (eg, viral load, CD4 counts). Reporting HIV results to public health is not within the scope of this checklist item.*~~

Evidence of Compliance:

✓ Patient reports with initial screening results and reflexive testing results and/or guidance

REFERENCES

1) Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Available at http://stacks.cdc.gov/view/cdc/23447. Published June 27, 2014. Accessed 11/19/2019.
2) National Center for HIV/AIDS, Viral Hepatitis, and TB Prevention (US). Divisions of HIV/AIDS Prevention; Association of Public Health Laboratories. 2018 Quick reference guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens. Available at: https://stacks.cdc.gov/view/cdc/50872. Published January 2018. Accessed 4/2/2023.
3) Association of Public Health Laboratories. Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm. January 2019. Available at APHL Publications. Accessed 11/19/2019.

BLOOD GAS ANALYSIS

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CHM.33900 Collateral Circulation Phase II

For radial artery sampling, a test for collateral circulation is performed before arterial puncture~~, as applicable~~ if clinically indicated, with results recorded.

NOTE: ~~The~~Any of the various technologies ~~available have been~~ evaluated in the published literature are acceptable. Consensus should be established between the laboratory and involved clinicians to define situations that require testing for collateral circulation, ~~including preferred technique(s) and situations in which such a test is medically useful in averting potential patient/client injury. The site from where the sample was obtained must be recorded~~if any, to potentially avert patient injury.

Evidence of Compliance:

✓ Records of collection site and results of applicable collateral circulation testing

REFERENCES

1) Vaghadia H, *et al*. Evaluation of a postocclusive circulatory hyperaemia (PORCH) test for the assessment of ulnar collateral circulation. *Can J Anaesth.* 1988;35:591-598
2) Cheng EY, *et al*. Evaluation of the palmar circulation by pulse oximetry. *J Clin Monit.* 1989;5:1-3
3) Levinsohn DG, *et al*. The Allen's test: analysis of four methods. *J Hand Surg.* 1991;16:279-282
4) Fuhrman TM, *et al*. Evaluation of collateral circulation of the hand. *J Clin Monit.* 1992;8:28-32
5) Furhman TM, *et al*. Evaluation of digital blood pressure, plethysmography, and the modified Allen's test as a means of evaluating the collateral circulation to the hand. *Anaesthesia.* 1992;47:959-961
6) Fuhrman TM, McSweeney E. Noninvasive evaluation of the collateral circulation to the hand. *Acad Emerg Med.* 1995;2:195-199
7) O'Mara K, Sullivan B. A simple bedside test to identify ulnar collateral flow. *Ann Intern Med.* 1995;123:637
8) Starnes SL, *et al*. Noninvasive evaluation of hand circulation before radial artery harvest for coronary artery bypass grafting. *J Thorac Cardiovasc Surg.* 1999;117:261-266
9) Cable DG, *et al*. The Allen test. *Ann Thorac Surg.* 1999;67:876-877