

TESTING FOR VIRAL HEPATITIS

The OHIP Laboratory Requisition contains a section to facilitate the ordering of tests related to viral hepatitis. It is important for clinicians to understand the tests performed when this part of the requisition is utilized.

There are three check boxes on the requisition labeled

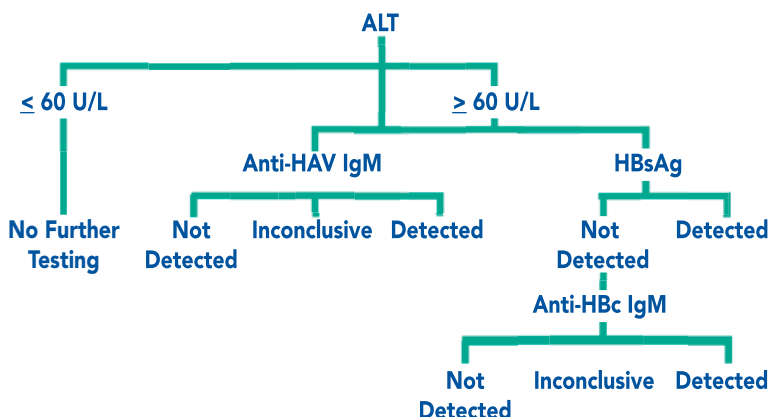
- Acute Hepatitis
- Chronic Hepatitis
- Immune Status/Previous Exposure

Acute Hepatitis

Acute hepatitis should be checked to investigate a patient with the clinical picture of acute hepatitis when viral hepatitis is part of the differential diagnosis. A testing algorithm is followed by the laboratory based on ALT as the sentinel test to exclude or document possible acute hepatitis. When ALT is less than or equal to 1.5x the upper reference limit, acute hepatitis is effectively excluded and no further testing is undertaken. The following message will appear on the report:

“ALT is less than or equal to 1.5x upper reference limit, no testing for acute viral hepatitis markers done.”

When ALT is greater than 60 U/L, testing for Hepatitis A and B markers is performed as illustrated below.



It follows the algorithm may:

- Not support a diagnosis of acute hepatitis (ALT 60 U/L or less).
- Support a diagnosis of acute hepatitis (ALT > 60 U/L).

Due to:

- Hepatitis A
- Hepatitis B
- Neither of the above

or

- Generate results which are inconclusive for either Hepatitis A or B.

The following points should be considered.

Acute Hepatitis should not be checked to detect a carrier of Hepatitis B. HBsAg should be specifically ordered in writing for a carrier may not have an elevated ALT in which case testing for the surface antigen would not be undertaken.

Anti Hepatitis C (Anti-HCV) will not be reliably detected during the acute phase of Hepatitis C. A sample should be specifically tested for Anti-HCV one to three months later to exclude or confirm Hepatitis C as the cause of acute hepatitis.

Repeat testing for Hepatitis A or Hepatitis B should be requested when results are reported as inconclusive. For Hepatitis B this will occur when Anti-HBc IgM is detected or the analysis is inconclusive. Interpretive messages will be appended when the need for further testing is apparent based on the initial analytical results.

Chronic Hepatitis

Chronic Hepatitis is persistent for more than six months. To investigate possible viral etiology the “Chronic Hepatitis” box on the OHIP requisition should be checked. The laboratory will test for HBsAg and for Anti-HCV. A positive HBsAg is consistent with either acute or chronic infection. To document chronic Hepatitis B with certainty the HBsAg should be persistent for at least six months.

Positive Anti-HCV indicates either recent or persistent infection with the Hepatitis C virus.

IN THIS ISSUE

TESTING FOR VIRAL HEPATITIS1	CHANGES TO TOTAL IGE REPORTING 4	HBA ₂ REFERENCE INTERVAL UPDATE..... 5	THE FINER POINTS OF SPECIMEN PACKAGING – (PUN INTENDED) 6
HELP! RADIOACTIVE URINE..... 2	THE REVISED LABORATORY REQUISITION 4	QUANTITATION OF 72-HOUR FECAL FATS DISCONTINUED.....5	CONTROL OF ORAL ANTICOAGULATION: PRACTICAL ADVICE FOR THE PHYSICIAN BASED ON FREQUENTLY ASKED QUESTIONS 7
UNEXPECTED AND UNEXPLAINED LAB RESULTS..... 2	MDS INTRODUCES CELIAC DISEASE SEROLOGY TESTING 5	LIPID TARGET VALUES UPDATED.....6	

Immune Status/Previous Exposure

A check box is included on the requisition to facilitate documentation of immune status to Hepatitis A or Hepatitis B.

Immune status for Hepatitis A is assessed by the measurement of total Anti-HAV. There are three possible results: Detected (positive), not-detected (negative) or inconclusive.

The first result documents either natural infection or previous immunization against Hepatitis A, the second indicates no previous infection or immunization, and the inconclusive or equivocal result requires repeat testing.

It is important to note detection of total Anti-HAV considered in isolation cannot differentiate acute Hepatitis A from immunity to the virus because Anti-HAV IgM will be detected. For this reason, whenever acute Hepatitis A is a clinical concern "Acute Hepatitis" must be checked in which case testing specific for Anti-HAV IgM will be performed.

Immune status for Hepatitis B is assessed by measurement of Anti-HBs.

Detection of the antibody indicates either previous infection or immunization. In some individuals who have been immunized or infected antibody titres may fall below the levels determined arbitrarily to indicate immunity yet effective immunity may persist.

On the revised OHIP requisition (July 2007) there is a check box "Hepatitis C" to facilitate the ordering of Anti-HCV as a single test.

Hepatitis B Contacts

Sexual and close contacts of newly diagnosed Hepatitis B carriers should be tested to determine if they are the source of infection or are immune or susceptible to Hepatitis B infection.

HBsAg and anti-HBs should be ordered by checking Immune status Hepatitis B, ordering HBsAg in writing and indicating "Hepatitis B contact" on the requisition. ■

HELP! RADIOACTIVE URINE

Patients who receive I¹³¹ are managed in hospital using protocols which maintain radiation safety and are instructed how to protect those living close to them upon discharge.

I¹³¹ which has a half life of 8 days is concentrated in the urine so patients are instructed to flush twice after urination and to wash carefully.

In the last year, without warning, we have received three specimens for urinalysis from patients treated for thyroid cancer using I¹³¹ in the recent past.

This may put our staff at risk. Since the empty containers cannot be submitted as biohazardous waste, we also face major difficulty and expense when they are inadvertently mixed with routine laboratory waste and radioactivity is detected prior to disposal resulting in rejection of the entire batch.

Please do not order investigations on urine from patients recently administered I¹³¹ and please ask such patients to warn other clinicians of the fact.

There can be few indications for investigation using urine at this time after administration of I¹³¹. If such investigation is contemplated you should discuss this with a medical director at MDS. ■

UNEXPECTED AND UNEXPLAINED LAB RESULTS

Laboratory test results are an invaluable tool for the clinician. They may confirm a clinical impression, direct further investigation in the differential diagnosis of a symptomatic patient or help determine the need for a change in therapy or a dose of a drug. They may be part of a program to screen healthy populations or patients at risk for a particular disease. On occasion, abnormal test results may come as a surprise because they do not relate well to the clinical impression. Clinical evaluation and repeat testing will usually clarify the significance for an individual patient. There will be occasions when, after a re-evaluation, the clinical picture and apparently abnormal laboratory results do not correlate. In this situation the possibility of mis-identification of a patient or sample must always be considered as well as the points noted below.

Factors important in the interpretation of laboratory results and which may impact the actual result are highlighted in the following table.

Variable	Explanation	Comment
Patient uniqueness	<ul style="list-style-type: none"> Reference ranges reflect the central 95th percentile of a normal healthy population. Statistically, 2.5% of healthy patients will have results that will be above and 2.5% will have results below the reference range. 	The further the result is from the limits of the reference range, the more statistically significant it becomes.
Biological Variation	<ul style="list-style-type: none"> Some tests, such as triglycerides, TSH, and CK have marked intra-individual biological variation (>10%). 	Consult with MDS Medical Director for further details.
Patient Preparation	<ul style="list-style-type: none"> The fasting state is important for an accurate fasting blood sugar and lipid results. Patient must refrain from eating specific foods for some tests to ensure result accuracy. Examples include 5-HIAA and Fecal Occult Blood. 	Patient non-compliance may be a contributing factor to unexpected results.
Time since last dose for drugs	<p>Therapeutic Drug Monitoring (TDM)</p> <ul style="list-style-type: none"> Samples drawn soon after last dose may be artificially high and not reflect the true equilibrium drug level. <p>Drugs of Abuse (DOA)</p> <ul style="list-style-type: none"> Unexpected “negative” results for DOA may be due to the length of time of urine collection after last use. The detection of DOA in urine is dependent on a number of factors, including the half-life of the particular drug, frequency and amount of drug used, as well as physiological. 	<p>Proper interpretation of drug results must always be made with the time since last dose as a point of reference. It is important to record this information on the patient requisition to avoid unnecessary late night calls for apparent critical results.</p> <p>Also refer to the “Drugs of Abuse Urine Testing” article in the October 2001 edition of MDS Lab News.</p>
Sample collection	<ul style="list-style-type: none"> Incorrect sample collection, using the improper type of tube used to collect the sample can significantly affect some tests. An example is the significant decrease in calcium results when collected in EDTA tubes. Incorrect order of draw of samples can affect some test results. One example is potassium can be artificially elevated in a sample collected in an SST tube right after a potassium EDTA (lavender) tube. 	<p>Incorrect sample collection due to wrong tube type can go undetected in some situations when the lab receives specimens in secondary tubes.</p> <p>MDS has published a document (Specimen Requirement Chart) outlining the correct order of draw process to be used.</p>
Sample preparation and storage	<ul style="list-style-type: none"> Samples remaining uncentrifuged for extended periods of time, even if refrigerated, will significantly alter some tests. For example, glucose results will decrease, while potassium, magnesium, ammonia, LDH, AST, ALT, and ferritin results will increase. 	<p>If delivery to the testing lab is delayed greater than 4 hours, eliminate contact of serum with Red Blood Cells, by centrifugation of specimen.</p> <p>To avoid a decrease in glucose due to glycolysis, a gray top tube should be used for the collection.</p>
Interferences	<ul style="list-style-type: none"> The extent of interference by hemolysis, icterus, and lipemia is well documented for the majority of lab tests. The effect of each on different tests is variable and may or may not be clinically significant. Interference by circulating endogenous heterophilic antibodies on immunoassays, used in the measurement of hormones, peptides, therapeutic drugs, viral antigens and antibodies, auto-antibodies, may increase results in some assays, but decrease results in others. There is a potential for interference due to the similarity in 3-dimensional structure to the analyte in question. For example, prednisone interferes with cortisol assays and some prescription drugs interfere with some Drug of Abuse assays. 	<p>Some tests are not reported in the presence of one or more of these interferences, while others are.</p> <p>Analysis of the sample by an alternative method can help to resolve unexpected results. Consult with MDS Medical Director for further details.</p> <p>Also refer to the “False Immunoassay Results due to Interfering Antibodies” article in the June 2002 edition of MDS Lab News.</p>
Specificity	<ul style="list-style-type: none"> Alternatively, some drugs may be structurally similar but may not be equally detected by the same method. For example, Opiate screening tests may be specific for Morphine and Codeine, but not detect Oxycodone. 	Consult with MDS Medical Director for further details.
Analyte heterogeneity	<ul style="list-style-type: none"> Analyte heterogeneity, from one patient to another, is most significant for hormones and peptides. Examples of this heterogeneity include genetic variation and macro-molecules, such as Macroprolactin. Due to the use of monoclonal antibodies, with differing specificities, in methods used to measure hormones and peptides, this heterogeneity can cause an analyte to be detected by one method but not another. 	Consult with MDS Medical Director for further details.

CHANGES TO TOTAL IGE REPORTING

In June 2007, MDS will implement a change to the technology for the assessment of Total IgE. The new technology is the Pharmacia ImmunoCAP 250.

Prior to the change, MDS reported Total IgE in units of $\mu\text{g/L}$. MDS will now report results in units of kU/L , the same units used to report the Specific IgE Allergens. In order to convert a result from $\mu\text{g/L}$ to kU/L , multiply the result by the factor 0.417. Alternatively, to convert a result from kU/L to $\mu\text{g/L}$, multiply the result by 2.4. Along with the change to the method and units used, the Total IgE reference ranges will be changed accordingly. ■

THE REVISED LABORATORY REQUISITION

An updated version of The Ontario MOHLTC Laboratory (OHIP) Requisition is to be released for use at the end of June 2007. The new requisition incorporates changes to the upper portion used to identify both patients and clinicians and to the lower portion used to order tests.

In the lower portion there are changes to the tests listed by name, to the organization of the sections, in particular Biochemistry and Microbiology, and to the layout of the sections.

The upper portion used to identify the patient, the ordering clinician and request copies be sent to other physicians has also undergone significant change. Some of these such as the inclusion of CPSO number are in anticipation of the introduction of the Ontario Laboratory Information System (OLIS) or reflect the requirement for confident and unique identification of patients and test samples as an important component of patient safety by preventing medical error.

A number of points are worth noting

The name provided should be that on the OHIP (Health) card and should include the middle name when applicable. You will see there is now a field for middle name. The use of familiar names by patients and your staff will be problematic when OLIS is introduced and you should be aware of this and require the use of the Health Card in your office to record the names of patients.

A field has been included to provide a contact number for the communication of results which are requested as urgent. This should not be a fax number not already validated by the laboratory.

A section has been added to identify clinicians to receive copies of the results. Either the full address or OHIP practitioner number

should be provided in this area or a copy cannot be forwarded.

The Public Health Laboratory (PHL) will not accept OHIP requisitions. A separate PHL requisition should be completed for tests performed by Ontario Public Health Laboratories and when cytology or pathology tests are required.

In the lower portion of the form the listed tests have been increased. It is now easy to indicate whether a glucose sample is random or fasting (or both) and HbA1C is included immediately below Glucose.

“Lipid Assessment” as a single check box orders the recommended profile to assess risk and monitor the effects of management. Individual tests may be ordered in writing.

ALT has replaced AST in the Biochemistry section as the most appropriate enzyme to monitor the liver and the one which for several years has been the sentinel test when “Acute Hepatitis” is checked on the requisition.

Sections are included to provide information critical to the interpretation of Neonatal Bilirubin and Therapeutic Drug levels. You or your staff should complete these sections and ensure patient contact information is provided in case another practitioner has to contact the patient or the parents of a neonate when specimens are procured outside of the laboratory collection system.

The Immunology Section still allows the order of only urine pregnancy tests. When serum hCG is required this must be ordered in writing in the “Other Test” section.

The Microbiology Section is expanded to allow specific ordering of Group B Strep Culture, Stool Ova and Parasites and more precise indication of the source of specimens for culture.

Clinicians responsible for the procurement of specimens should note the fields to enter date and time of specimen collection. This information is important for purpose of interpretation and helps document proper specimen handling.

We believe the updated requisition will be an improvement once users are familiar with the changes included. ■

MDS INTRODUCES CELIAC DISEASE SEROLOGY TESTING



Celiac disease or gluten sensitive enteropathy (GSE) is characterized by chronic inflammation of the small intestinal mucosa, villous atrophy and flattening of the epithelium. Intolerance to gluten, the protein of wheat, rye and barley, causes GSE. Patients with celiac disease may suffer from diarrhea, malabsorption, anemia, fatigue, and other diverse side effects, or they may be asymptomatic. Dermatitis herpetiformis (DH) is a skin disease associated with GSE. All GSE patients have an increased risk of lymphoma. A gluten-free diet controls GSE and associated risks.

Several antibodies, including endomysial and gliadin antibodies, have been identified in the pathology of celiac disease and DH. The endomysial antigen has been identified as the protein cross-linking enzyme known as tissue transglutaminase (tTG). Gliadin is the alcohol soluble fraction of wheat gluten, and is the toxic agent in the disease.

Serological tests have a high sensitivity and specificity for the detection of untreated celiac disease, but small intestinal biopsy remains the gold standard for confirmation of the diagnosis.

In May 2007, MDS implemented celiac disease testing, including anti-Transglutaminase IgA, anti-Gliadin IgA and anti-Gliadin IgG evaluations. All 3 tests are performed using an ELISA technology. Turnaround time is 48-72 hours.

In Ontario, none of these tests are covered by OHIP, but may be covered by private insurance schemes. ■

HbA₂ REFERENCE INTERVAL UPDATE

Effective June 4, 2007, MDS will report a revised reference interval for HbA₂. A review of data indicated that the upper limit of the reference range should be adjusted resulting in a range of 0.020-0.032. Any HbA₂ value above this reference range will be referred to a hematopathologist for interpretation and comment. ■

QUANTITATION OF 72-HOUR FECAL FATS DISCONTINUED

Fecal fats, measured after a 72-hour collection, is a nonspecific test used in the diagnosis of malabsorption and steatorrhea. MDS has received notification that the reference laboratory presently completing requests for this assay have discontinued testing effective May 31. For this reason, MDS can no longer offer this test.

Interpretation of the test results due to patient non-compliance to the diet prior to collection, the challenges associated with sample collection, and analytical performance have rendered the test of limited value in many cases.

Initial investigation of possible malabsorption syndrome based on clinical assessment of the symptoms may be carried out using alternative simple biochemical tests.

The initial screening test for malabsorption is a qualitative examination of random stool for undigested neutral fats and meat fibers. Examination of the stool for neutral fats has a sensitivity of 80-90% for detection of significant steatorrhea. A negative result does not, however, exclude steatorrhea. Other assays and the expected result in malabsorption are summarized in the following table:

Assay name	Expected Result In Malabsorption
Stool fat (qualitative)	Increased
Stool meat fibers	Increased
Serum iron	Decreased
Serum albumin	Decreased
Serum folate	Decreased
Serum calcium	Decreased
Serum beta carotene	Decreased
CBC and smear	Anemia, Macrocytosis
PT/INR	Increased

REFERENCES

- Hill PG. Fecal fat: time to give it up. *Ann. Clin. Biochem.* 2001; 38: 164-167.
- Thomas PD *et. al.* Guidelines for the investigation of chronic diarrhea, 2nd, Ed., Gut 2003 : 52(V) v1-v15.

LIPID TARGET VALUES UPDATED

In September 2006, the Canadian Cardiovascular society published an updated position statement with recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease (CVD). In developing the revised guideline the working group established primary and secondary review panels and used a guidelines research and evaluation process to grade the evidence available for each recommendation.

No changes in the process to identify the individual patient's 10-year risk of CVD were made, however lipid target values for select patient populations were revised. The following table summarizes the revised target for each risk category. Changes in lipid treatment target are highlighted in bold text.

Supplemental tests which may be of interest include measurement of apolipoprotein B (Apo B). Risk of CVD is highest in patients with an Apo B > 1.20 g/L and triglyceride level > 1.50 mmol/L. Increased Apo B and triglyceride concentrations are often seen in patients with type 2 diabetes. Quantitation of Apo B may also be valuable in assessing adequacy of statin treatment performed when serum ALT and CK are measured to monitor potential side effects.

The table summarizes the optimal concentration of Apo B in patients who are at high risk, moderate or low risk.

For detailed discussion of the guideline, frequency of testing, other supplemental assays and treatment options please refer to referencelisted below ¹.

Risk	10-year risk score for CVD	Target Values		Supplemental tests Apolipoprotein B
	%	LDL-C (mmol/L)	TC/HDL-C ratio	g/L
High Or patients with diabetes, atherosclerotic disease, renal failure	≥20%	< 2.00	< 4.0	< 0.85
Moderate	11% - 19%	≤ 3.50	≤ 5.0	< 1.05
Low	≤10%	≤ 5.00	≤ 6.0	< 1.20

Clinicians have indicated they do not wish to have the chart of target values printed on each of our reports. The document can be accessed at www.mdsdx.com together with a printable pdf form of the Framingham risk assessment tables used to assign risk category for individual patients based on age, sex, blood pressure, total cholesterol and HDL-cholesterol. This is also available on the OAML website (www.oaml.com). The online version of the risk assessment tool can be located at http://www.oaml.com/calculator/Lipids_Calculatorrev06012007.pdf. ■

REFERENCES

- McPherson R. et.al. Canadian Cardiovascular Society position statement – Recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. Can. J. Cardio 2006; 22(11) 913-927.

THE FINER POINTS OF SPECIMEN PACKAGING – (PUN INTENDED)



A loose syringe, with needle attached, was recently sent to our laboratory from a physician's office. This clearly placed all individuals who handled the package, including our staff, at risk of a needle stick by a contaminated needle. This is an occurrence we work very hard to avoid.

Although in the overwhelming majority of cases specimens from physicians are packaged appropriately, it is vitally important all clinician offices follow appropriate guidelines and train staff to follow these and consider the safety of others.

Please note that no loose "sharps" such as needles or blades are to be sent to our laboratory under any circumstances. For those physicians who collect blood specimens on our behalf, an approved disposal container is provided for safe disposal. The lid must be securely closed and locked in place prior to being returned to our staff. ■

CONTROL OF ORAL ANTICOAGULATION: PRACTICAL ADVICE FOR THE PHYSICIAN BASED ON FREQUENTLY ASKED QUESTIONS

Warfarin dosing and management of non-therapeutic INR results

The use of oral anticoagulants is increasing steadily. This is due to the increasing prevalence of atrial fibrillation as the population ages, and to the increasing incidence of deep venous thrombosis. Given warfarin's narrow therapeutic window, it is essential that physicians become very familiar with all aspects of oral anticoagulant dosing. The intent of this article is not to provide a complete review but to provide practical advice that will help you in your everyday practice caring for patients in the community. This should result in better protection against thrombosis, and decrease the incidence of bleeding complications.

Question 1: What is the starting dose of warfarin?

The use of loading doses >10 mg/day to achieve a rapid rise in the INR (International Normalized Ratio) is generally contraindicated. Current guidelines suggest a dose between 5 and 10 mg. However, lower doses are recommended for the elderly and for patients with concurrent illnesses or taking medications (which may increase the anticoagulant effect of warfarin). As can be seen in the table below, the maintenance dose of warfarin decreases with age. Therefore, it is safer to initiate warfarin with doses close to the age-specific average maintenance dose.

Effect of Age on Warfarin Maintenance Doses

Patient Age	Mean Warfarin Daily Dose (mg)				
	<50	50-59	60-69	70-79	>80
Gurwitz, et al, 1992 <i>(n=530 patients total study)</i>	6.4	5.1	4.2	3.6	ND
James, et al, 1992 <i>(n=2,305 patients total study)</i>	6.1	5.3	4.3	3.9	3.5

Question 2: How often should the INR be checked?

Obtain a baseline PT/INR/APTT (to screen for underlying coagulopathies). Repeat the INR after 2-3 doses of warfarin. Outpatients, can be tested twice a week, then weekly for 2-3 weeks, then once every 4 weeks providing stable INRs are achieved.

Question 3: How to adjust warfarin doses for sub therapeutic INR results? And is the rate of rise of the INR important to monitor?

It is important to distinguish between the initiation and maintenance phases of oral anticoagulation when considering a change in warfarin dose. Keep in mind that because of warfarin's long half-life of 36 hours, there is a delay before the full effect of an ingested dose is seen. The initiation phase is the first 7-10 days of therapy. After the first 2-3 doses one should look for a slight increase in INR (0.1-0.3 units) above baseline. If not seen, then the dose should be increased slightly (15-25%). On the other hand, a rapidly rising INR indicates an overdose, and dose reduction is mandatory (25-75%). As a guide, consider that most patients, receiving appropriate doses, will achieve an INR of 2.0 by 5-7 days on average.

Question 4: What is the difference between the therapeutic INR range and the target INR value?

The therapeutic range defines the minimum and maximum acceptable INR values (e.g. 2.0-3.0, or 2.5-3.5). The target value is the INR value in the middle of that range (e.g. 2.5, and 3.0 respectively). In adjusting warfarin doses one should aim for the target value. Of course it is impossible to be exactly at this value, but patient's results, in the maintenance phase, should oscillate around this value. It is normal for INR results to fluctuate slightly even when everything else remains constant. Therefore, a patient whose INR is repeatedly 2.0 or 2.1 actually risks being below 2.0 for a significant period of time, and requires a slight increase in warfarin dose. The same applies to values that are repeatedly close to the upper limit of the therapeutic range, where slight dose decreases would be necessary.

Question 5: How should high INR results be managed? When is vitamin K necessary?

A distinction should be made between patients with no or only minor bleeding, and those with serious bleeding. In addition, large doses of vitamin K (>5 mg) will make the patient temporarily relatively warfarin resistant (7-10 days). Higher warfarin doses will be necessary until this period of resistance is over. At such a time, physicians should anticipate reducing the warfarin dose back to baseline, or risk causing over-anticoagulation.

Managing Patients with High INR Values/Minor or No Bleeding

Clinical Situation	Guidelines
INR > therapeutic range but < 5.0, no clinically significant bleeding, rapid reversal not indicated for reasons of surgical intervention	Lower the dose (10-15%) or omit the next dose; resume warfarin therapy at a lower dose (10-15%) when the INR approaches desired range. If the INR is only minimally above therapeutic range, dose reduction may not be necessary.
INR > 5.0 but < 9.0, no clinically significant bleeding	<p>Patients with no additional risk factors for bleeding: omit the next dose or two of warfarin, monitor INR more frequently, and resume warfarin therapy at a lower dose (10-20%) when the INR is in therapeutic range.</p> <p>Patients at increased risk of bleeding: omit the next dose of warfarin, and give vitamin K₁ (1 to 2 mg orally).</p> <p>Patients requiring more rapid reversal before urgent surgery or dental extraction: vitamin K₁ (2-4 mg orally); if the INR remains high at 24 h, give an additional dose of 1-2 mg.</p>

It is also important to note that given warfarin's long half life, repeat doses of vitamin K may be necessary in cases of warfarin overdose. The two tables in this section were developed from guidelines published by the American College of Chest Physicians (ACCP), and the American Heart Association, and apply to patients in the maintenance phase of anticoagulation. ■

Managing Patients with Very High INR Values/Serious Bleeding

Clinical Situation	Guidelines
INR > 9.0, no clinically significant bleeding	Vitamin K ₁ (2.5 mg orally); closely monitor the INR; if the INR is not substantially reduced by 24-48 h, the vitamin K ₁ dose can be repeated.
Serious bleeding, any INR	Patient should be referred immediately to the nearest emergency room.

REFERENCES

1. Ansell J, et al. The pharmacology and management of the vitamin K antagonists. The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-based Guidelines. Chest 2004; 126 (3 suppl): 204S-233S.
2. Gurwitz JH, et al. Aging and the anticoagulant response to warfarin therapy. Ann Int Med 1992; 116: 901-904.
3. James AH, et al. Factors affecting the maintenance dose of warfarin. J Clin Path 1992; 45: 704-706.
4. American Heart Association. www.americanheart.org.

For more information, CONTACT:

Dr. Frank Thompson
Medical Director, Ontario
416-675-4530 ext. 4209
frank.thompson@mdsdx.com

Dr. Sheila Boss
Scientific Director, Ontario
416-675-4530 ext. 2296
sheila.boss@mdsdx.com

Dr. Peter Catomeris
Clinical Biochemist
416-675-4530 ext. 2029
peter.catomeris@mdsdx.com

Dr. Wahbi Hammouda
Director of Laboratory Hematology
416-675-4530 ext. 2728
wahbi.hammouda@mdsdx.com

Dr. Deborah Yamamura
Medical Microbiologist
416-675-4530 ext. 2344
deborah.yamamura@mdsdx.com