

## Feature

### Diagnosis and Monitoring of Multiple Myeloma

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## Diagnosis and Monitoring of Multiple Myeloma

### What is Multiple Myeloma?

Multiple myeloma is a cancer that originates in the bone marrow and develops from malignant plasma cells. The American Cancer Society estimates that there will be 14,600 new cases of multiple myeloma in 2002.<sup>1</sup> The disease accounts for 10% of all malignant hematologic neoplasms, is difficult to detect in early stages, and current therapies are not curative.<sup>2</sup>

Roughly one-third of the patients seen by hematologists at Mayo Clinic with a myeloma diagnosis were asymptomatic when the disease was first detected. These patients are designated as asymptomatic myeloma, smoldering myeloma (M-spike present but stable), or indolent (slowly progressing) myeloma. As the disease progresses, the malignant plasma cell population grows and interferes with the formation of normal blood components in the bone marrow, eventually leading to a shortage of red blood cells, white blood cells, and platelets. The resulting anemia and leukopenia frequently present with clinical symptoms of hemorrhage, fatigue, and recurrent infections.<sup>1,2</sup>

Overstimulated by tumor cells, osteoclasts (which break down bone in the normal process of bone remodeling) destroy bone tissue without the normal corresponding bone formation. The excessive breakdown of the bone results in lesions that appear to have been punched out of the bone. (See Photo 1.) These characteristic lesions form on the bones in approximately 66% of myeloma patients. If the cancer is advanced, the bone loss may reach a degree where the patient suffers fractures easily.

### What is Monoclonal Gammopathy of Undetermined Significance?

A monoclonal gammopathy is defined by the proliferation of a single clone of lymphoid or

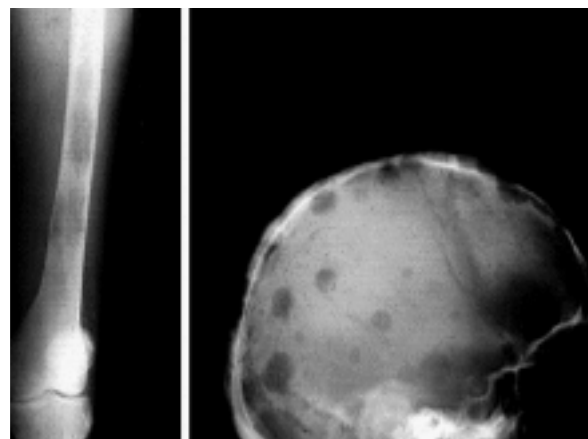
plasma cells. Individuals with monoclonal gammopathy of undetermined significance (MGUS) have a monoclonal protein in their serum, but the diagnostic criteria for multiple myeloma are not present. When a plasma cell abnormality is detected early, it is important to distinguish between multiple myeloma and MGUS. Prognosis and treatment for MGUS is quite different from myeloma and the physician needs to differentiate between them to select the best course of care. Approximately 20-25% of patients with MGUS will progress to multiple myeloma. Survival rates vary widely and early evaluation of prognostic factors may assist in therapy selection.<sup>2</sup>

### Identification and Diagnosis

Patients with early myeloma are usually asymptomatic. Early symptoms of myeloma are nonspecific and may be attributed to other diseases. Generalized bone pain, anemia, numbness or limb weakness, symptoms of hypercalcemia, and recurrent infections are all symptoms that may indicate myeloma.

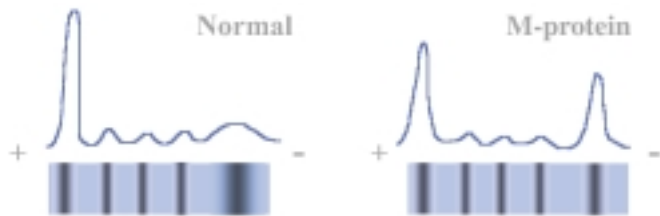
Asymptomatic patients may be identified during a routine physical examination when blood or

Photo 1. Classic bone lesions of multiple myeloma.



urine tests (protein electrophoresis) detect a monoclonal protein spike, a low hemoglobin level, or an elevated total protein level. (See Figure 1.)

Figure 1. Protein electrophoresis identifies the presence of a monoclonal protein spike.



When there is a clinical suspicion of myeloma, the first steps are laboratory tests and x-rays. *Multiple Myeloma: A Simplified Algorithm* (Figure 2) provides an overview to the diagnostic features of multiple myeloma. An *Expanded Algorithm for the Laboratory Evaluation of Multiple Myeloma* (Figure 3 - page 5) provides a detailed guide for the laboratory evaluation of multiple myeloma.

### Imaging Studies

Imaging studies are performed to detect bone destruction caused by the tumors. Cytokines released by the tumor cells stimulate bone absorption,

weakening the bone and creating lesions. Standard x-rays can detect these changes. However, magnetic resonance imaging (MRI) also may be performed, as it provides a more detailed image capable of detecting changes in bone structure before it is visible by x-ray examination.<sup>1</sup> More than half of multiple myeloma patients develop the characteristic bone lesions observed on the skull, vertebrae, pelvis, and appendicular skeleton.

### Laboratory Tests

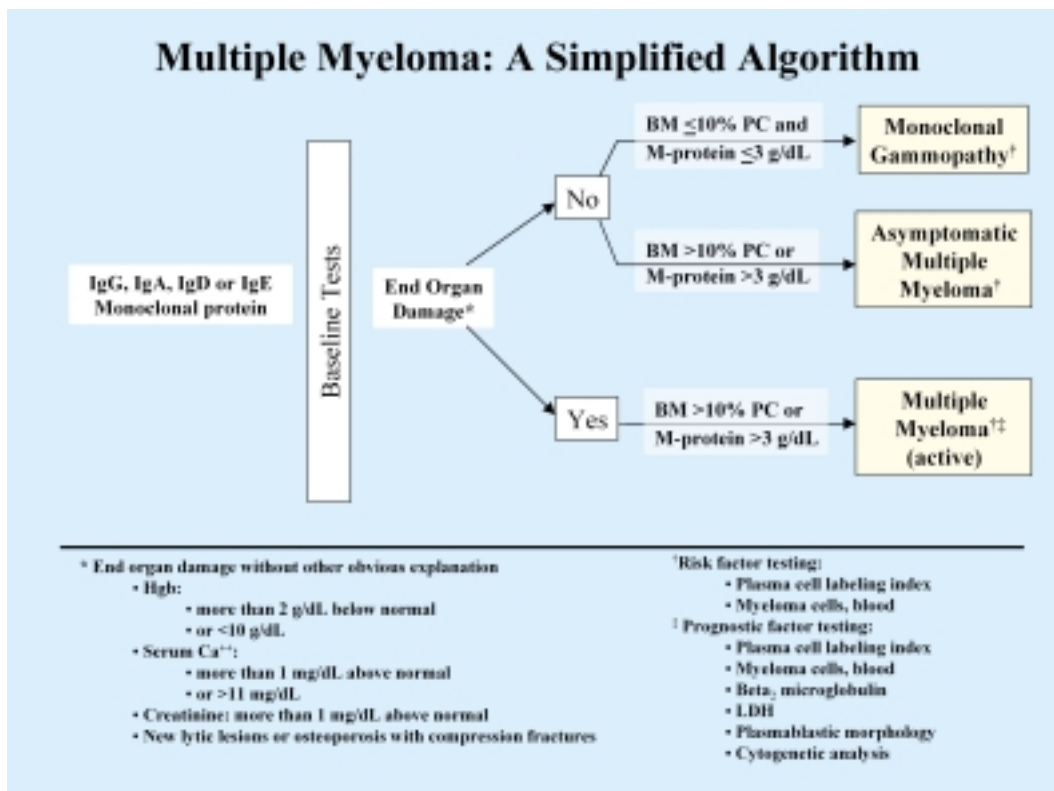
#### Blood and Urine Studies

##### High-Resolution Electrophoresis

[Monoclonal Protein Study, Serum #81756](#) and [Monoclonal Protein Study, Urine #8823](#) include protein electrophoresis, heavy-chain typing, and light-chain typing (kappa and lambda). High-resolution electrophoresis is a screening test used to identify the accumulation of abnormal proteins (also known as: monoclonal immunoglobulin, monoclonal [M-] protein, M-spike, or paraprotein). High-resolution serum or urine electrophoresis can identify the accumulation of these proteins, represented by a spike in the gamma globulin region.<sup>1,3</sup>

The laboratory evaluates the protein electrophoresis results and performs immunofixation to characterize the

Figure 2. Multiple Myeloma: A Simplified Algorithm



M-protein.<sup>3,4</sup> When electrophoresis is negative, immunofixation may still be useful to detect small M-proteins.<sup>3</sup>

A monoclonal gammopathy is an indication of a clonal expansion of plasma cells. Depending on the type of protein, size of the M-protein peak, and the clinical symptoms, the identification of a monoclonal gammopathy may be consistent with:<sup>4</sup>

- MGUS
- multiple myeloma
- primary systemic amyloidosis
- lymphoproliferative disease
- macroglobulinemia

#### Circulating Plasma Cells

Normal patients usually have no circulating plasma cells. Mayo Medical Laboratories (MML) offers [Myeloma Cells, Blood #9302](#), for detection of circulating plasma cells. The number of circulating monoclonal plasma cells is an indication of a monoclonal gammopathy.

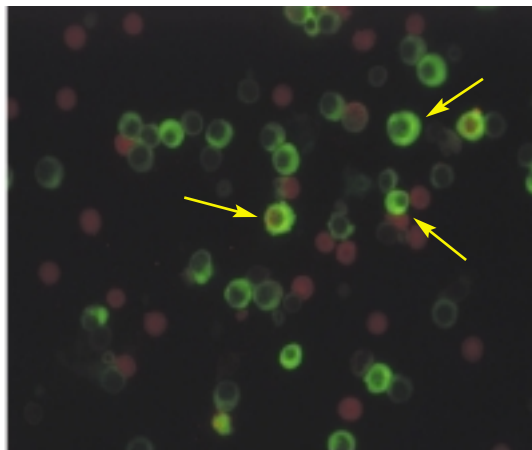
<u>Circulating Plasma Cell Count</u>	
<4% of Ig positive cells or <4 x 10 <sup>6</sup> /L	≥4% of Ig positive cells or ≥4 x 10 <sup>6</sup> /L
Inactive myeloma	Active multiple myeloma*
Smoldering myeloma	
MGUS	
Treated multiple myeloma	

\*may require treatment

When circulating plasma cells are present in patients with newly diagnosed multiple myeloma, the number of cells is an adverse prognostic factor for survival. Additionally, circulating plasma cell levels correlate with a shorter time-to-progression from smoldering myeloma to active myeloma. Circulating plasma cell levels also correlate with disease activity and a high percentage of abnormal circulating cells is associated with poor prognosis.<sup>2</sup>

Blood plasma cells are detected by first screening whole blood with 2-color flow cytometry using antibodies to CD38 and CD45. The remainder of the blood is subjected to Ficoll-Paque separation, mononuclear cells are isolated, and cytospin slides are made. Antibody to cytoplasmic kappa- or lambda-light chain is applied to the slides and they are reviewed using immunofluorescence microscopy. (See Photo 2.) Plasma cells are identified by their morphology and cytoplasmic light-chain restriction. The immunofluorescent microscopy confirms that CD38+/CD45- events detected by flow cytometry are indeed light chain restricted and that they have plasma cell morphology.

Photo 2. Immunofluorescent study measures the percent of plasma cells in the peripheral blood. Under fluorescence, plasma cells are green (see arrowed cells-not all plasma cells are arrowed).

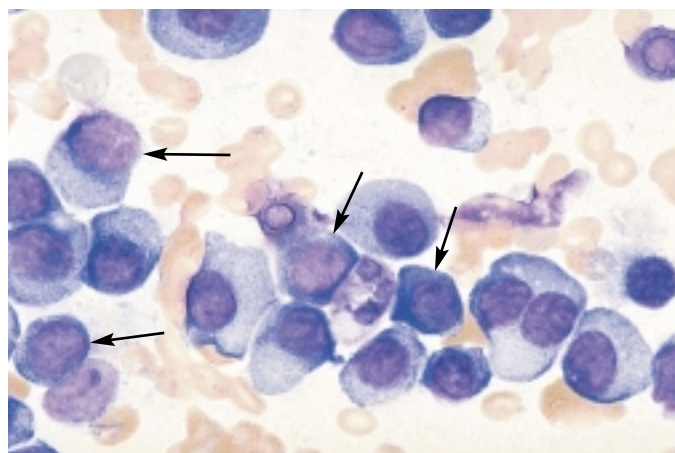


#### **Bone Marrow Studies**

##### Plasmablastic Morphology Evaluation

A plasmablast is a precursor cell of a plasma cell. Plasmablastic morphology evaluation is performed on bone marrow aspirate slides as [Bone Marrow Biopsy #9172](#). When 2% or more of the cells present demonstrate the features of plasmablasts, the specimen is considered to have plasmablastic morphology. Based on a Mayo Clinic study, plasmablastic morphology is prognostic of poor survival after either standard chemotherapy or autologous transplantation.<sup>2,5</sup> (See Photo 3.)

Photo 3. Plasma cells with plasmablastic features are identified by arrows.



##### Plasma Cell Labeling Index and S-phase Estimation Tests

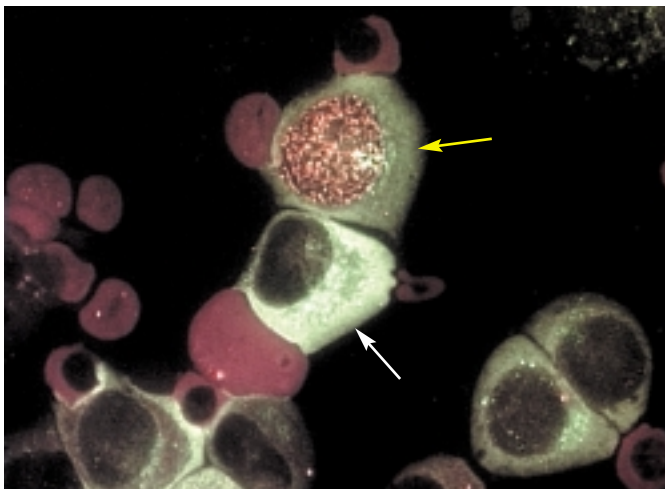
The [Plasma Cell Labeling Index \(LI\) #8217 \(PCLI\)](#) quantitates the proportion of plasma cells that are actively dividing and is therefore a measure of disease activity. (See Photo 4.) The immunofluorescent PCLI is a rapid, reliable method that can be used to distinguish

patients with overt active multiple myeloma from MGUS, asymptomatic multiple myeloma, and patients in relapse from those in plateau phase of multiple myeloma. The immunofluorescent PCLI has also proven to be an independent prognostic indicator and measure of disease activity. A high PCLI value, >1.0%, suggests active disease with a greater than 90% certainty. PCLI values of this magnitude are associated with a 5-year survival probability of 13%, while PCLI values of <1% are associated with a 5-year survival probability of 41%.

The PCLI test utilizes a monoclonal antibody to 5-bromo-2-deoxyuridine (BrdU) and fluorescein isothiocyanate conjugated kappa and lambda light chain antisera to identify monoclonal plasma cells. In specimens with a low plasma cell percent or atypical plasma cells, PCLI allows easier, more accurate identification of these cells than S-phase estimation (DNA synthesis phase).

The S-phase estimation test (by flow cytometry) also quantitates the proportion of plasma cells that are actively dividing. While the S-phase test identifies a larger proportion of the actively dividing cells compared to PCLI, PCLI has the advantage of being more informative in specimens with less than 20% plasma cells in the bone marrow.<sup>2</sup> A high PCLI (>1%) or a high S-phase (>3%) both identify patients with a poor prognosis.<sup>2</sup> PCLI is the preferred test at Mayo.

Photo 4. Plasma cell labeling index measures the incorporation of BrdU into S-phase nuclei of plasma cells (see yellow arrow), visible using a fluorescence microscope. Plasma cells that are not in S-phase also fluoresce, but do not accumulate BrdU (see white arrow).



### Tests of Prognostic Value

There are numerous factors that have prognostic value in multiple myeloma. The widely used Durie-Salmon staging system uses blood calcium levels, serum or urine protein levels, blood hemoglobin concentration, and creatinine concentration.<sup>1,2</sup> Some physicians prefer to use a 2-factor system, staging the patient based on serum albumin and beta<sub>2</sub> microglobulin levels.<sup>1</sup> Other factors that can be utilized to refine the prognosis include bone marrow PCLI, S-phase estimation, cytogenetic analysis, plasmablastic morphology, lactate dehydrogenase (LDH) levels, and C-reactive protein.<sup>1,2</sup>

#### Beta<sub>2</sub> Microglobulin

Beta<sub>2</sub> microglobulin is a small, light chain protein that is an established predictor of survival.<sup>2</sup> Serum level of beta<sub>2</sub> microglobulin has a demonstrated correlation with myeloma tumor burden and values >4 µg/mL are considered a negative prognostic factor.<sup>4</sup> Beta<sub>2</sub> microglobulin is an established predictor of post-treatment survival after conventional chemotherapy and also an independent predictor of post-transplant survival.<sup>2</sup> [Beta-2-Microglobulin \(Beta<sub>2</sub>-M\), Serum #9234](#) is performed by nephelometry.

#### IL-6 and sIL-6R

Interleukin-6 (IL-6) is a normally occurring growth factor and is required in the development of normal plasma cells. However, in the presence of malignant plasma cells, IL-6 induces a significant proliferative response, driving a rapid increase in the number of malignant cells.<sup>2</sup> At elevated levels, soluble interleukin-6 receptors (sIL-6R) amplify the stimulatory effect of IL-6 on malignant plasma cells by a factor of up to 10-fold. High levels of either IL-6 or sIL-6R are predictors of poor outcomes. These tests are currently under investigation at Mayo for their potential role in myeloma monitoring.

#### C-Reactive Protein

C-reactive protein (CRP) is an acute phase reactant that is easily assayed and has been proposed as a surrogate for IL-6 testing by some groups.<sup>2</sup> CRP is produced by hepatic cells in response to IL-6 levels. Therefore, the level of CRP is proportional to the level of IL-6. However, further studies are needed to demonstrate that CRP is an independent prognostic factor in myeloma outcomes. [C-Reactive Protein \(CRP\), Serum #9731](#) is performed as a latex particle-enhanced immunoturbidimetric assay.

#### Lactate Dehydrogenase

Serum levels of lactate dehydrogenase (LDH), orderable as [Lactate Dehydrogenase, Serum #8344](#), may be elevated

A **REVISED** Expanded Algorithm for the Laboratory Evaluation of Multiple Myeloma

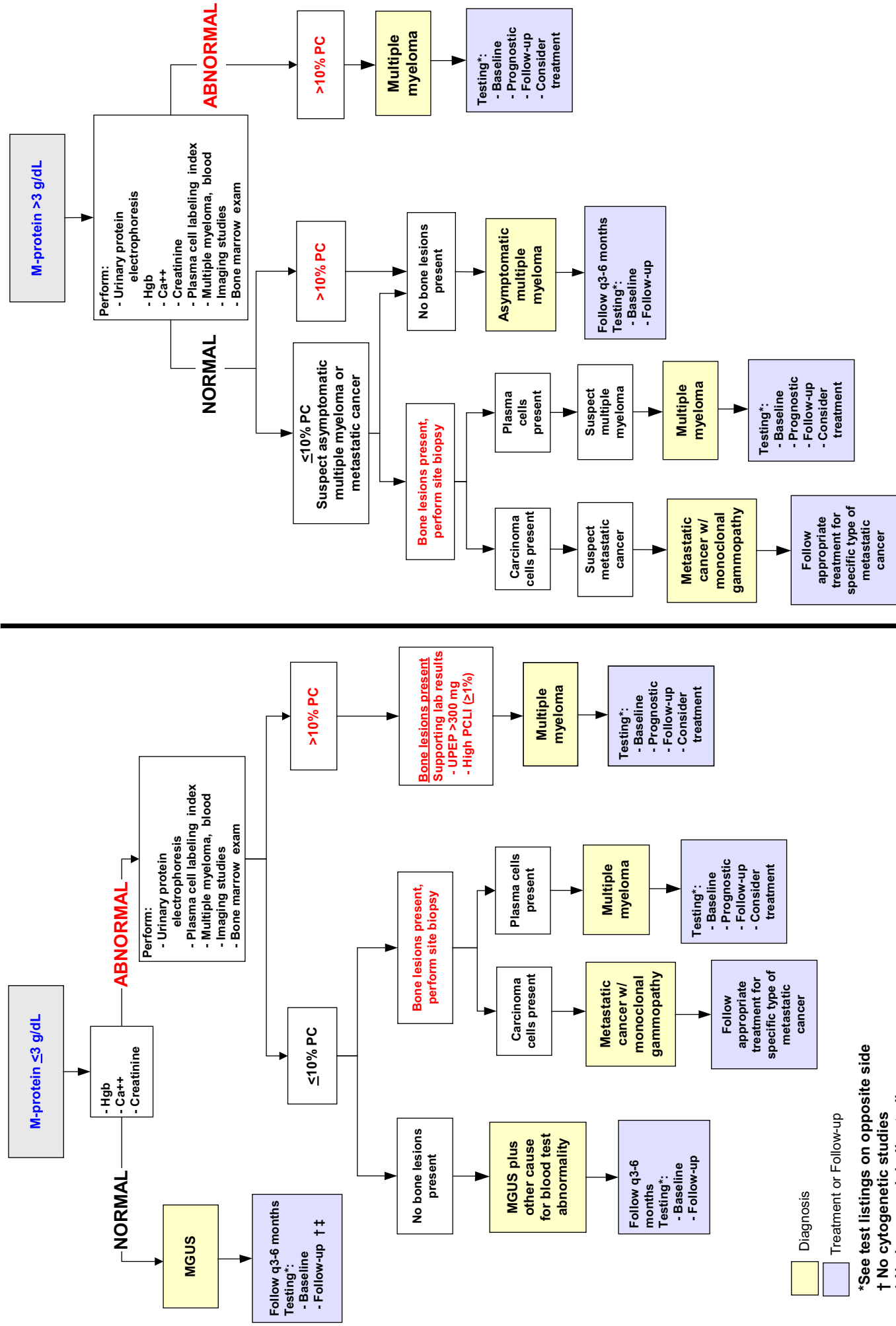


Figure 3

■ Diagnosis

■ Treatment or Follow-up

\*See test listings on opposite side

† No cytogenetic studies

‡ No immunoglobulin studies

**A REVISED Expanded Algorithm for the Laboratory Evaluation of Multiple Myeloma**

**PLEASE REPLACE THE ALGORITHM IN YOUR FEBRUARY ISSUE WITH THIS REVISED ALGORITHM.**

**THIS REVISION INCORPORATES CHANGES FOR THE DIAGNOSIS OF ASYMPTOMATIC MULTIPLE MYELOMA**

<u>Baseline Tests:</u>	<u>Prognostic Tests:</u>	<u>Follow-up Tests:</u>	<u>Ancillary Tests:</u>
- hemoglobin (Hgb)	- beta <sub>2</sub> microglobulin	- SPEP	- PCLI
- serum protein electrophoresis (SPEP)	- plasmablastic morphology evaluation (bone marrow)	- UPEP	- myeloma cells
- urine protein electrophoresis (UPEP)	- LDH	- Ca <sup>++</sup>	- magnetic resonance imaging (optional)
- calcium (Ca <sup>++</sup> )	- myeloma cells	- creatinine	
- creatinine	- plasma cell labeling index (PCLI)	- CBC	
- complete blood count (CBC)	- cytogenetic analysis-standard	- beta <sub>2</sub> microglobulin	
- beta <sub>2</sub> microglobulin	- cytogenetic analysis-FISH (for research only)	- C-reactive protein	
- C-reactive protein		- myeloma cells	
- myeloma cells (circulating neoplastic plasma cells)		- IgA or IgG	
- lactate dehydrogenase (LDH)			
- cytogenetic analysis-standard			
- cytogenetic analysis-FISH (for research only)			
- immunoglobulin testing (A,M,G)			
- bilirubin			
- glucose			
- sodium			
- potassium			
- uric acid			

**Algorithms are designed to assist in the investigation and monitoring of disease. Due to the evolutionary nature of medical science, algorithms evolve and change over time. This algorithm is designed to be used in conjunction with clinical judgment, based on the clinical presentation of the patient.**

in numerous clinical conditions.<sup>4</sup> Very high levels are seen in megaloblastic anemias, Hodgkin's disease, abdominal and lung cancers, and high levels have been associated with an aggressive presentation of myeloma.<sup>2,4</sup> As a rule, the elevations of LDH in patients with cancer are too erratic to be of use in clinical diagnosis, although serum levels have been assayed to monitor changes in tumor burden after chemotherapy.<sup>4</sup> However, elevations of these enzymes are found in only a small number of patients with myeloma and, therefore, the assay has limited application for staging or monitoring myeloma.<sup>2</sup>

#### Bone Remodeling Markers

Osteoclasts are involved in the process of resorption. As plasma cell tumors proliferate substances are released that activate osteoclasts, resulting in areas of bone weakness.<sup>1</sup> As the bone is resorbed at a higher rate than it is formed, high levels of calcium build up in the blood.

Serum markers of bone metabolism have been studied in clinical trials led by Mayo investigators to determine whether there is a relationship between the markers, the presence of bone manifestations, and survival.<sup>6</sup> The five markers, osteocalcin, carboxy-terminal propeptide of type I collagen, bone alkaline phosphatase (BAP), carboxy-terminal telopeptide of type I collagen, and tartrate-resistant acid phosphatase show potential as prognostic markers.<sup>6</sup> Further studies will be necessary to identify the best applications for these markers.

#### Cytogenetic Analysis

Cytogenetic analysis, [Chromosome Analysis for Hematologic Disorders, Bone Marrow #8506](#) or [Chromosome Analysis for Hematologic Disorders, Blood #8537](#), identifies chromosome abnormalities associated with malignancies. However, cytogenetic analyses rarely detect abnormalities in newly diagnosed myeloma patients because of the small proportion of dividing neoplastic plasma cells.<sup>2</sup> A much higher rate of detection is seen in patients who have relapsed.<sup>2</sup> Mayo hematologists routinely order cytogenetic analysis prior to bone marrow transplantation on multiple myeloma patients and there is a growing trend among hematologists to order cytogenetic analysis for baseline evaluation of myeloma patients.

Certain cytogenetic abnormalities, specifically abnormalities of chromosome 11 and 13, have been associated with poor myeloma outcomes.<sup>2</sup> Deletion 13 is considered a prognostic indicator for multiple myeloma.

Fluorescence *in situ* hybridization techniques (FISH) are being actively investigated for use in detecting

immunoglobulin heavy-chain gene translocations.<sup>2</sup> (See Photos 5-7.) Because FISH technology does not rely on active division for analysis, results are promising, with abnormalities detected in 65% of multiple myeloma patients who had a normal conventional cytogenetic result.<sup>2</sup> The FISH tests are currently for research only but are expected to become an orderable test in the not-so-distant future.

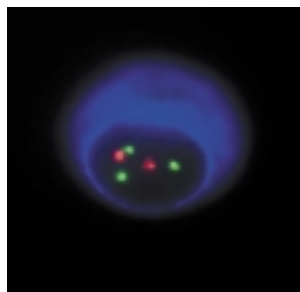


Photo 5. Trisomy 7: each green signal indicates the presence of a chromosome 7.

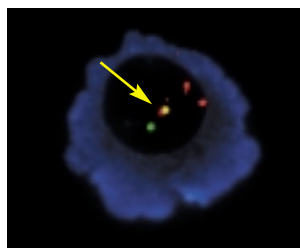


Photo 6. Translocation  $t(11;14)$ : the translocation fusion product shows as a combined red/yellow signal (see arrow).

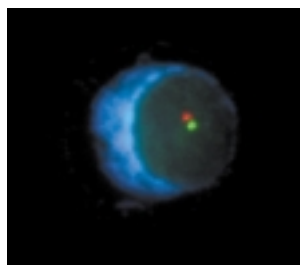


Photo 7. Chromosome 13 deletion: 2 different colored probes are used to test for the loss of a portion of the chromosome 13q-arm (13q-). Normal cells contain 2 red and 2 green signals-1 of each color on a normal chromosome. In this cell, both signals are missing from 1 chromosome, indicating the deletion of the critical portion of the 13q-arm.

### Summary

While there is no cure for myeloma at this time, clinical trials and other research projects are focused on identifying ways to deal with this cancer. Meanwhile, physicians have a growing number of tests available to them to help in the early identification, staging, and monitoring of the myeloma patient. The laboratory plays a key role in the diagnosis and management of multiple myeloma.

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### Tumor Microsatellite Instability Method Change

**Tumor Microsatellite Instability #82500** utilizes immunohistochemical staining and polymerase chain reaction (PCR) testing to help establish the diagnosis of hereditary nonpolyposis colorectal cancer (HNPCC) for high-risk individuals.

The PCR-based portion of the assay is used to test for tumor microsatellite instability (MSI). Recently, the method was converted from a gel electrophoresis-based detection method to capillary electrophoresis (ABI 3100). Capillary electrophoresis requires significantly less personnel time and eliminates the use of radioactive substances.

## Lipid Testing Reference Values Changed

MML will discontinue reporting the age-adjusted reference values for the lipid tests listed below. The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) recently adopted new criteria for classification of lipid measurements. These classifications now have been adopted by MML and are included as reference values for these tests.

Test Code #	Title
8053	Lipid Panel
7973	Calculated LDL (only orderable through 8053)
8316	Triglycerides, Serum
8320	Cholesterol, Total, Serum
8429	Cholesterol, HDL, Serum
8409	Lipoprotein Profile, Serum (includes 8316 and 8320)

### New Reference Values

#### Total Cholesterol:

Desirable:	<200 mg/dL
Borderline high:	200-239 mg/dL
High cholesterol:	≥240 mg/dL

#### LDL Cholesterol:

Optimal:	<100 mg/dL
Near/above optimal risk:	100-129 mg/dL
Borderline high	130-159 mg/dL
High:	160-189 mg/dL
Very high:	≥190 mg/dL

#### HDL Cholesterol:

Low HDL:	<40 mg/dL
Normal:	40-59 mg/dL
Desirable:	≥60 mg/dL

#### Triglyceride:

Normal triglycerides:	<150 mg/dL
Borderline high:	150-199 mg/dL
High:	200-499 mg/dL
Very high:	≥500 mg/dL

Flags, high (H) and low (L) will be placed on the laboratory results as follows:

Total Cholesterol:	Flag High at ≥240 mg/dL
HDL Cholesterol:	Flag Low at <40 mg/dL
LDL Cholesterol:	Flag High at ≥160 mg/dL
Triglyceride:	Flag High at ≥200 mg/dL

## Abstracts of Interest

### PSA Doubling Time as a Predictor of Clinical Progression After Biochemical Failure Following Radical Prostatectomy for Prostate Cancer

Steven G. Roberts, MD; Michael L. Blute, MD; Erik J. Ergstralh, MS; Jeffrey M. Slezak; and Horst Zincke, MD, PhD

- **Objectives:** To characterize the clinical progression of disease in men who have undergone prostatectomy for clinically localized prostate cancer and have postoperative biochemical failure (elevated prostate-specific antigen [PSA] level) and to identify predictors of clinical disease progression, including the possible effect of PSA doubling time (PSADT).
- **Patients and Methods:** Between 1987 and 1993, 2809 patients underwent radical retropubic prostatectomy for clinically localized ( $\leq T2$ ) disease. In our database, all patients with postoperative biochemical failure (PSA level  $\geq 0.4$  ng/mL) were identified. The PSADT was estimated using log linear regression on all PSA values (excluding those values determined after administration of hormonal therapy) within 15 months after biochemical failure. All patients had regular PSA measurements from the time of surgery through the follow-up period. Systemic progression (SP) was defined as evidence of metastatic disease on a bone scan. Local recurrence (LR) was defined on the basis of digital rectal examination, transrectal ultrasonography, and biopsy. The SP-free survival and LR/SP-free survival (survival free of both LR and SP) after biochemical failure was estimated with use of the Kaplan-Meier method. Patients with prostate cancer treatment after biochemical failure had their follow-up censored from this study at the time of treatment.
- **Results:** Postoperative biochemical failure occurred in 879 men (31%). The mean follow-up from time of biochemical failure was 4.7 years (range, 0.5-11 years). The mean time to biochemical failure was 2.9 years (median, 2.4 years). The overall mean SP-free survival from time of biochemical failure was 94% and 91% at 5 and 10 years, respectively. The mean LR/SP-free survival was 64% and 53% at 5 and 10 years, respectively. By using univariate analysis on the 587 patients with PSADT data, significant risk factors for SP were PSADT ( $P < .001$ ) and pathologic Gleason score ( $P = .005$ ); for LR/SP, significant risk factors included PSADT ( $P < .001$ ) and pathologic Gleason score ( $P < .001$ ). In multivariate Cox models analysis, only PSADT remained a significant risk factor for both SP and LR/SP ( $P < .001$ ). Mean 5-year SP-free survival was 99%, 95%, 93%, and 64% for patients with PSADT of 10 years or longer, 1.0 to 9.9 years, 0.5 to 0.9 year, and less than 0.5 year, respectively; the respective mean LR/SP-free survivals were 87%, 62%, 46%, and 38%. The percentage of patients with PSADT of less than 0.5 year was considerably higher if the type of first clinical event was SP (48%) compared with LR (18%) ( $P < .001$ ).
- **Conclusions:** For patients who have undergone radical prostatectomy, a rising PSA level suggests evidence of residual or recurrent prostate cancer. Many men remain free of clinical disease for an extended time after biochemical failure following radical prostatectomy for clinically localized prostate cancer. The PSADT appears to be an important predictor of SP and also of any clinical progression (local or systemic). These data may be useful when counseling men regarding the timing of adjuvant therapies.

Mayo Clinic Proceedings 2001;76:576-581

Ask



US

**Q:** Why doesn't MML offer an islet cell antigen assay?

**A:** Islet cell antibodies are assayed for several reasons:

1. Assessing susceptibility to autoimmune (type 1, insulin-dependent) diabetes mellitus and related endocrine disorders (eg, thyroiditis and pernicious anemia).
2. Distinguishing between patients with type 1 and type 2 diabetes.
3. Confirming a diagnosis of stiff-man syndrome and autoimmune cerebellitis

MML's [Glutamic Acid Decarboxylase \(GAD65\) Antibody Assay, Serum #81596](#) is a comparable test for the above indications. Additionally, the GAD65 assay is far more sensitive than islet cell antibody assays.

The GAD65 assay is a double antibody immunoprecipitation assay using 125I-labeled recombinant human protein, which corresponds to the 65-kDa isoform of glutamic acid decarboxylase found in pancreatic beta islet cells and GABAergic neurons in the brain. GAD65-specific antibodies account for most, but not all, antibodies detected in the islet cell antibody tests. The assay was developed and validated at Mayo Clinic.

The GAD65 assay detects antibodies in low titer (0.03-20 nmol/L) in the serum of 76% of patients who have insulin-dependent (type 1) diabetes mellitus. GAD65 also accurately detects antibodies in 93% of patients with the rare stiff-man syndrome, where patients have high titers (>20 nmol/L). High titers are also seen in patients with acquired (autoimmune) cerebellar ataxia. Additionally, positives in lower titer are seen in ~20% of patients with autoimmune neuromuscular disorders, such as myasthenia gravis and Lambert-Eaton myasthenic syndrome.

Mayo is currently developing an insulin antibody test, which is more specific for type 1 diabetes, but less sensitive than GAD65 Ab.

## Communiqué

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# Meeting Calendar

## *Interactive Satellite Program . . .*

February 12, 2002

Advances in the Management of Rheumatoid Arthritis

Presenters: Harvinder Luthra, MD & Alexander Ruggieri, MD - Moderator: Steven Ytterberg, MD

March 12, 2002

The Prevention & Management of Type 2 Diabetes

Presenter: Mehmood Khan, MD - Moderator: Robert Kisabeth, MD

April 23, 2002

Complementary & Alternative Medicine: From Traveling Medicine Shows to the Internet and the NIH

Presenter: Brent Bauer, MD - Moderator: Robert Kisabeth, MD

September 17, 2002

Advances in Wound Healing

Presenter: Steve Kavros, DPM - Moderator: Robert Kisabeth, MD

October 22, 2002

Bone Marker Assays: Are They Useful for the Diagnosis & Treatment of Osteoporosis?

Presenter: Lorraine Fitzpatrick, MD - Moderator: Robert Kisabeth, MD

November 19, 2002

HIV Update

Presenter: Zelalem Temesgen, MD - Moderator: Robert Kisabeth, MD

December 10, 2002

Stroke Prevention and Management

Presenter: David Wiebers, MD - Moderator: Robert Kisabeth, MD

## *Upcoming Education Conferences . . .*

### Practical Spirometry

March 12-13, 2002

Mayo Clinic, Siebens Building  
Rochester, Minnesota

September 13-14, 2002

Holiday Inn Chicago City Centre  
Chicago, Illinois

October 31-November 1, 2002

Mayo Clinic, Siebens Building  
Rochester, Minnesota

Course Director: Paul D Scanlon, MD  
Presented by Mayo Pulmonary Services

### Integration Through Community Laboratory Insourcing: From Mission Statement to Successful Implementation

May 1-3, 2002

Hilton in the WALT DISNEY WORLD, Resort  
Lake Buena Vista, Florida  
Course Director: Rodney Forsman

### Quality Issues in Phlebotomy

October 10-11, 2002

Mayo Clinic, Siebens Building,  
Rochester, Minnesota

Course Co-Directors: Linda Iverson & Sharon Wiesner

**Presented by Mayo Medical Laboratories**

For additional information regarding the above programs, please contact the  
Mayo Reference Services Education Office at 1-800-533-1710 or 507-284-8742.





February 2002

# *For Your* INFORMATION

A Mayo Reference Services Publication



## Pathology Consultation

### Submitting Specimens and X-ray Films to Mayo Medical Laboratories

Timely review of your pathology specimens/x-ray films is a priority for Mayo Medical Laboratories (MML). To expedite your Pathology Consultation, we request that you send specimens/x-ray films via Federal Express, Airborne Express (Standard or Priority Overnight Delivery), or MML Courier to the following address:

**Dr. \_\_\_\_\_ (Pathologist's name, if known)**  
**Mayo Medical Laboratories**  
**Attention: Pathology**  
**200 First Street SW**  
**Rochester, MN 55905**

When this address is used, your specimens/x-ray films are delivered directly to our pathology laboratory receiving area. If you do not identify a specific pathologist, your specimen will be triaged and forwarded to the most appropriate specialist.

Pathology specimens/x-ray films sent via other carriers (eg, U.S. Postal Service, United Parcel Service) are delivered to a different receiving area and may not be available for pathologist review until the following working day. Your cooperation in addressing these specimens appropriately will ensure the most rapid routing of your consultation to our pathologists. For your convenience, we provide color-coded (green), preaddressed mailing labels. These labels may be ordered from MML Packaging as Supply T498.

To expedite the processing of your consultation request, please include the following materials:

1. For verification of correct patient identification we require:
  - a) MML Request form
  - b) copy of the preliminary report with the full patient name, date of birth, and slide/block numbers
  - c) brief explanatory note
2. Hematoxylin-and-eosin (H&E) stained slides.
3. When appropriate, please include special stained slides, unstained slides, paraffin blocks, or pathology x-ray films. If the need for special studies is anticipated, appropriate tissue specimens should be sent as follows:
  - Electron microscopy: glutaraldehyde-fixed or, if necessary, formaldehyde-fixed tissue.
  - Special staining methods: paraffin blocks for most stains. A few stains require frozen tissue.
  - Pathology x-ray films: if shipped with blocks/slides, please place these materials inside the x-ray film envelope and ship all items in one package.
4. If pathology x-ray films are sent separately, include a copy of your preliminary pathology report and a brief explanatory note.

If you have any questions regarding this information or wish to order the green color-coded, preaddressed mailing labels, please call us at 1-800-533-1710.

*The green color-coded labels are for use with pathology specimens/x-ray films only. Please note that x-ray films submitted to Mayo Medical Imaging for second opinion should be shipped utilizing blue Mayo Medical Imaging mailing labels.*

Anatomic Pathology Mailing Label

\_\_\_\_\_  
Name

\_\_\_\_\_  
Address

\_\_\_\_\_  
City/State/Zip

**Mayo Medical Laboratories**  
Attention: Pathology  
200 First Street SW  
Rochester, MN 55905

T498

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