



April 2009

### **Bone Marrow Biopsies in the Elderly**

A study published in the November 2008 issue of the American Journal of Clinical Pathology examined the usefulness of performing bone marrow biopsies in patients 85 years or older. Researchers from the Department of Pathology at the University of Iowa retrospectively reviewed all bone marrow biopsy cases from January 2002 to December 2006 for patients 85 years or older at the time of biopsy. A total of 119 cases were reviewed. Indications for biopsy and the percentages of cases for each category are listed in the table below:

**Bone Marrow Biopsy Indications in  
119 Cases of Patients ≥ 85 Years**

Indication	Number (%)
Cytopenias (1 or more)	43 (36.1)
Follow-up of a previously diagnosed myelodysplastic syndrome (MDS) or MDS-transformed acute myelogenous leukemia (AML)	14 (11.8)
Suspicion of plasma cell myeloma (PCM)	13 (10.9)
Follow-up of previously diagnosed PCM	10 (8.4)
Thrombocytosis or leukocytosis	17 (14.3)
Follow-up/staging of known lymphoma/chronic leukemia	13 (10.9)
Suspicion for lymphoma	6 (5.0)
Other	3 (2.5)

After excluding cases that resulted from follow-up or staging of known malignancies, 79 of 119 cases remained. A specific diagnosis was determined in only 34 (43%) of the 79 cases.

Although cytopenia, especially anemia, was the most common indication for biopsy in this age group, it was the least likely to generate a specific diagnosis. Of the cases in which a specific diagnosis was determined, MDS accounted for 11 cases, myeloproliferative disorder for 10 cases, multiple myeloma for 5 cases, acute leukemia for 3 cases and lymphoproliferative disorder for 3 cases.

Chart reviews showed that only 20 of 45 patients for whom follow-up information was available received disease-modulating therapy. Of those receiving therapy, 17 patients received abbreviated or modified therapies due to poor therapeutic response or medication intolerance. Therapy failures were reported in all patients.

The authors concluded that because a specific diagnosis was not determined in many cases, few patients received more than supportive therapy following bone marrow biopsy for cytopenias and because of the potential for increased morbidity in this population, a higher threshold for bone marrow biopsy may be indicated in the 85 or older age group.

### **TB Update**

A recent issue of MMWR (Volume 58, #10;249-253) reviews trends in tuberculosis in the United States for 2008. Overall, the rate of TB infection in 2008 was the lowest since national reporting began in 1953. North Dakota reports the lowest TB rate (0.5 cases per 100,000 population), while Hawaii has the highest (9.6 cases per 100,000 population). In comparison, Missouri and Kansas have case rates of <2.0 and 2.0-4.0 per 100,000 population, respectively. Four states (California, Florida, New York, & Texas) accounted for approximately half the 2008 TB cases, and each of those states reported more than 500 cases. A total of 12,898 cases were reported.

Foreign-born persons account for a disproportionate number of U.S. TB cases. Persons from four countries (Mexico, the

Philippines, India, & Vietnam) represent the majority of those cases. Racial/ethnic minorities are also encumbered with TB rates 8-23 times higher than whites, with Asians having the highest number of cases. TB rates declined among all groups in 2008.

Drug resistance continues to be of concern in TB. Multidrug-resistant TB (MDR TB) is defined as resistance to at least isoniazid and rifampin. The rate of MDR TB has remained stable, but is disproportionately higher among foreign-born persons (82% of MDR TB). Extensively drug-resistant TB (XDR TB) is defined as resistance to isoniazid, rifampin, fluoroquinolones, and at least one injectable drug (amikacin, capreomycin, or kanamycin). XDR TB has been reported in the U.S. since 1993, with four cases in 2008. The CDC recommends that TB prevention & control capacity should be increased to ensure that TB rates continue to decline in the U.S.

### Heparin-Induced Platelet Antibody Test

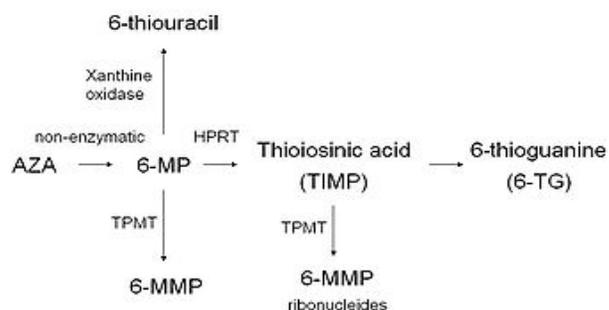
Effective May 1, Saint Luke's Regional Laboratories will change the methodology for testing for heparin-induced platelet antibodies. The new method detects IgG isotype antibodies by an ELISA method, and has higher specificity than the current method. Qualitative results will be reported (as negative or positive) based on an optical density (OD) cut-off of 0.50. The actual OD value will also be reported. Patients with OD values between 0.30 and 0.50 may benefit from repeat testing. Discrepancies between clinical suspicion of heparin induced thrombocytopenia and laboratory tests may occur; therefore, the results of this test must be interpreted in the clinical context.

### Thiopurine Methyltransferase Activity

Azathioprine (Imuran) and 6-mercaptopurine (Purinethol, 6-MP) are thiopurine drugs that are used to treat neoplasms such as acute lymphoblastic leukemia and a variety of rheumatologic, dermatologic, and neurologic diseases which are believed to have an immune etiology. Both drugs are metabolized to purine nucleotides, which are subsequently incorporated into DNA. This step is necessary for their antimetabolite activity and therapeutic efficacy.

The enzyme, thiopurine methyltransferase (TPMT), provides a competitive pathway for inactivation of these drugs by thiol methylation. A balance must be established between these 2 competing metabolic pathways such that sufficient drug is converted to 6-thioguanine to act as an antimetabolite, but the level does not become so high as to cause lethal bone marrow suppression.

Distinct inheritable differences in levels of red blood cell TPMT have been detected among patients. Patients with low or absent TPMT activity are at an increased risk of developing severe, life-threatening myelosuppression if conventional doses are given.



Approximately 10% of the population is heterozygous and 0.3% is homozygous for low TPMT activity. A reduced dose of azathioprine or 6-MP is recommended for heterozygous individuals, while alternative therapies should be considered for homozygous individuals.

Reference values are:

TPMT Level	Interpretation
15.1-26.4 U/mL RBC	Normal
6.3-15.0 U/mL RBC	Heterozygous low TPMT
<6.3 U/mL RBC	Homozygous low TPMT

Numerous patients have values which are near the cutoff between normal and the heterozygous state due to both assay variability and biological variation.

Specimen requirement is one 5 mL green-top (heparin) tube of whole blood. Specimen must be refrigerated and tested within 72 hours of draw.