

Putting the Puzzle Pieces Together: Making Sense of Tests & Results

Lab Tests, Bone Marrow Biopsy/Genetic Testing, and Imaging Studies

Debbie Birns IMF Medical Editor





What Tests Can Tell Us

- Is this myeloma, SMM, or MGUS?
- What is the risk of progression to myeloma?
- What are the type and stage of the myeloma?
- Are there genetic risk factors?
- Is the treatment working?
- Are treatments causing side effects?
- How deep is the response to therapy?

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Some Caveats

- No one test tells the whole story. Each test is a piece of a puzzle that must be assembled to understand what's going on.
- Don't compare results with other patients.
- If you have other medical problems, make sure you know which tests are for myeloma and which tests are for the other conditions.



More Caveats

- Always discuss results with the doctor who is treating you.
- Patterns of results viewed over time are more meaningful than any single test result in isolation.
- For some patients, certain tests are more important than others.

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Even More Caveats

- Normal lab values vary from lab to lab (LLN ULN).
- Test results can also vary from lab to lab.
- Factors having nothing to do with myeloma can affect test results.
- The units on lab values may also vary from lab to lab (grams, milligrams, liters, deciliters, etc.).
- Get and keep copies of your test results.

Major Types of Tests

• Laboratory tests to assess substances in blood and/or urine

- Complete Blood Count
- Blood chemistry/metabolic panel
 - Tests that assess kidney function
 - Tests that assess proteins and other substances in blood
- Tests that assess monoclonal protein
- Bone marrow tests
- Imaging studies



Tests to Assess Substances in Blood and/or Urine: Complete Blood Count (CBC)







Tests to Assess Substances in Blood and/or Urine: CBC

- Complete Blood Count (CBC)
- RBC (10¹²/L- billions per liter)
 - Hemoglobin: low hgb = anemia, the "A" ir the CRAB diagnostic criteria
- WBC (10⁹/L millions per liter)
 - Neutrophils target bacteria and fungi (IMiD effect: 1)
 - Lymphocytes target antigens and make antibodies (steroid effect: 1)
- Platelets (10⁹/L millions per liter)
 - Proteasome inhibitor effect:

	Test			Result		Flag	Reference
	HEMATOLOGY AUTOHEMATOLOGY - DIFFERENTIAL - MORPHOLOGY						
	CBC TREA	Т					
n	WBC				4.4		4.5-11.0 K/UL
	RBC				3.46		3.5-5.5 M/UL
	HGB				12.3		12.0-15.0 G/DL
	HCT				36.2		36.0-48.0 %
	MCV				104.6	Н	79.0-101.0 FL
	MCH				35.5	Н	25.0-35.0 PG
	MCHC				34.0		31.0-37.0 G/DL
	RDW-CV				15.8	ĺ	11.0-16.0 %
	PLT				149		140-440 K/UL
	MPV				7.5	1	7.0-10.0 Fl
	NEUT	8	(AUTO)		74		40-76 %
	LYMPH	00	(AUTO)		16	L	24-44 %
	MONO	8	(AUTO)		9		1.0-10.0 %
	EOS	S	(AUTO)		1		0.0-3.0 %
	BASO	8	(AUTO)		0	İ	0-1 %
	NEUT A	AB	(AUTO)		3.22	1	1.9-8.8 K/UL
	LYMPH 2	AB	(AUTO)		0.69	L	1.0-4.8 K/UL
	MONO	AB	(AUTO)		0.41		0.1-0.8 K/UL
	EOS 2	AB	(AUTO)		0.03		0.0-0.5 K/UL
	BASO	AB	(AUTO)		0.02		0.0-0.1 K/UL



Tests to Assess Substances in Blood and/or Urine Blood Chemistry/Metabolic Panel: Tests that Assess Kidney Function







Blood Chemistry/Metabolic Panel: Tests that Assess Kidney Function

- Kidney Function: the "R" in the CRAB Criteria)
 - Serum creatinine mg/dL
 - Waste product from normal muscle breakdown
 - Amount increases with kidney damage
 - Creatinine clearance mL/min
 - 24-hr urine + blood sample
 - More accurate than serum creatinine
 - Amount decreases with kidney damage





Blood Chemistry/Metabolic Panel: Tests that Assess Kidney Function

- Estimated glomerular filtration rate (eGFR) mL/min/1.73 m²
 - Usually calculated automatically along with creatinine clearance
- Blood urea nitrogen (BUN) mg/dL
 - Measurement of waste product in the blood when the body breaks down proteins; made in liver and eliminated by kidneys
 - Increases when kidneys or liver are damaged





– Calcium mg/dL – the "C" in the CRAB Criteria

- Indication of increased bone breakdown, increased risk for fracture
- Elevated calcium can cause kidney damage
- Total Protein g/dL (albumin and globulin)
 - Globulin: High globulin can indicate MM
 - Albumin: low level can indicate liver disease or kidney disease





- Serum beta 2 microglobulin (sβ2M) mg/L

- Monitoring disease activity and response to treatment
- Used in staging myeloma (prognosis)

- Lactate dehydrogenase (LDH) IU/L

- More LDH is released into the blood when tissues are damaged by injury or disease (i.e. by myeloma)
- Used in staging myeloma (prognosis)



- CRP (C-reactive protein) mg/L

- Produced by the liver in response to inflammation
- Higher levels indicate active MM
- Glucose mg/dL
- Should be assessed at diagnosis and throughout treatment that includes a steroid





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- Protein Electrophoresis- The "M-spike"
 - Serum Protein Electrophoresis (SPEP) g/dL
 - Separates proteins by electrical charge (α 1, α 2, β 1, β 2, gamma-where the M-spike is located)
 - Measures the amount, not the type, of monoclonal protein
 - IgA can be difficult to assess with SPEP
 - Darzalex[®] (daratumumab) slightly increases the amount of IgG
 - Urine Protein Electrophoresis (UPEP) mg/24 hrs
 - Separates proteins by electrical charge
 - Measures the amount of light chain protein in urine







• Immunofixation Electrophoresis (IFE) (yes/no)

- Presence or absence of monoclonal protein in blood or urine
- Identifies the types of monoclonal protein (heavy and/or light chain), but not the amount
- Complementary to SPEP (which gives the amount, but not the type of monoclonal protein)
- Read by a human being in the lab, not by a machine
- Darzalex will show up as a tiny band if the patient has IgG myeloma



• Quantitative Immunoglobulins (QIg) mg/dL

- Measures the total of each heavy chain antibody (Ig) type in the blood (IgG, IgA, IgM, IgD, IgE)
- Measures both polyclonal (normal) and monoclonal (abnormal) Ig's in one lump sum
- If an increase in an Ig is found, further testing is required



Serum Free Light Chain Assay (Freelite®)mg/L

- Diagnosis, prognosis, and monitoring
- Quantifies the light chains that are "involved" in the patient's myeloma and also the level of "uninvolved" light chains
- Measures the ratio between kappa and lambda chains (kappa ÷ lambda)
- Used for assessing risk of progression of MGUS and SMM





• Serum Heavy/Light Chain Assay (Hevylite®) g/L

- Measures intact immunoglobulins (light chains bound to heavy chains)
- Measures both involved and uninvolved Ig pairs (i.e. IgG kappa and IgG lambda; IgA kappa and IgA lambda)
- Read by a computer, not a human being
- Often used to measure IgA myeloma because IgA is difficult to quantify with SPEP





International Myeloma Foundation



Bone Marrow Tests

- Bone marrow aspiration and core biopsy
 - Performed at diagnosis and at doctor's discretion after treatment (especially post ASCT) and/or when needed to assess disease status
 - Tells what percent of the cells in bone marrow are abnormal plasma cells (i.e. myeloma cells)
 - Describes plasma cell appearance (may use terms like "mature," "immature," "atypical")





Bone Marrow Tests

- Flow Cytometry / Immunophenotyping
 - Important for determining sCR (stringent Complete Response) and MRD (Minimal Residual Disease)
 - Identifies myeloma protein markers if present on cells in bone marrow sample
 - Next Generation Flow[®] (NGF) developed through BSRI can detect 1 myeloma cell in 1 million plasma cells sampled

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Bone Marrow Tests

• Cytogenetics (karyotyping)

- Looks at chromosomes in dividing myeloma cells
 - Performed at diagnosis, sometimes after treatment, and at suspected relapse
 - Picks up high-risk mutations, especially fewer than two copies of each chromosome and loss of chromosome 13





Bone Marrow Tests

- FISH (Fluorescence In Situ Hybridization)
 - Complementary to cytogenetics
 - Each chromosome is identified by a different color
 - Identifies high-risk abnormalities such as translocations [t(4;14)] and deletions [17p-]





Imaging Tests





Imaging Studies

- Imaging studies assess the "B" in the CRAB Criteria
- X-ray
 - Still the standard of care in the US for bone imaging (but not for long)
 - Simple and inexpensive, but not sensitive
 - Shows bone thinning and bone loss, but not focal lesions (abnormalities in bone marrow)
 - Appearance of lytic lesions may not change even if there is no longer active myeloma
 - Exposes the patient to radiation



Imaging Studies

MR



MRI (Magnetic Resonance Imaging)

- Uses magnetic energy, not radiation
- Highly sensitive for detection of early bone involvement (focal lesions) before bone destruction occurs
- Can distinguish between benign vs malignant vertebral fractures
- Can detect spinal cord compression and soft tissue masses
- Not good for monitoring b/c it takes up to 9 months for healing to show
- May require contrast agent gadolinium potential problems



Imaging Studies

• CT (Computerized Axial Tomography)

- Cross-sectional, 3-dimensional x-ray
- More sensitive than x-ray for small lesions and soft tissue masses
- Exposure to radiation (although less with LDCT)
- Not good for monitoring because appearance of lytic lesions may not change even if there is no longer active myeloma
- May require contrast agents that pose problems for patients with kidney damage

PET (Positron Emission Tomography)

- Whole-body, real-time study
- Shows where cancer is actively growing in the body
- Used when patient has nonsecreting myeloma
- PET/CT = PET with CT of areas that "light up" on PET
- Used in diagnosis, therapy _ assessment, and prognosis
- Shows extramedullary disease —
- Included in IMWG MRD assessment _ criteria





• This has been a quick overview of the many tests that make up our puzzle. For more information on these tests, you can read the IMF's *Understanding Your Test Results* booklet, available on the IMF website at <u>www.myeloma.org</u> or in hard copy by calling the IMF at 800-452-2873.



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