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

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

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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?
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.
• 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.
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** ($10^{12}$/L - billions per liter)
    - Hemoglobin: low hgb = anemia, the "A" in the CRAB diagnostic criteria
  - **WBC** ($10^9$/L – millions per liter)
    - Neutrophils target bacteria and fungi (IMiD effect: ⬇️⬇️️)
    - Lymphocytes target antigens and make antibodies (steroid effect: ⬇️⬇️️)
  - **Platelets** ($10^9$/L – millions per liter)
    - Proteasome inhibitor effect: ⬇️⬇️️

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

- Creatinine
- Clearance
- BUN
- Serum Creatinine
- eGFR
- Complete Blood Count (CBC)

Red: Tests to assess blood cells
Purple: Tests to 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
Blood Chemistry/Metabolic Panel: Tests that Assess Blood Proteins, etc.

- Creatinine Clearance
- BUN
- Serum Creatinine
- eGFR
- Sβ2M
- LDH
- Calcium
- Glucose
- Total protein

Tests to assess blood cells
Tests to assess kidney function
Tests to assess blood proteins, etc.
Blood Chemistry/Metabolic Panel: Tests that Assess Blood Proteins, etc.

− **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
Blood Chemistry/Metabolic Panel: Tests that Assess Blood Proteins, etc.

- **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)
Blood Chemistry/Metabolic Panel: Tests that Assess Blood Proteins, etc.

- **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
Tests to Assess Substances in Blood or Urine:

Tests to Assess Monoclonal Protein

Tests to assess blood cells
Tests to assess kidney function
Tests to assess blood proteins, etc
Tests to assess monoclonal protein
Tests to Assess Substances in Blood or Urine: Tests to Assess Monoclonal Protein

- **Protein Electrophoresis**- The “M-spike”
  - **Serum Protein Electrophoresis (SPEP)**
    - g/dL
    - Separates proteins by electrical charge (α1, α2, β1, β2, 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
Tests to Assess Substances in Blood or Urine:
Tests to Assess Monoclonal Protein

• **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
Tests to Assess Substances in Blood or Urine: Tests to Assess Monoclonal Protein

- **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
Tests to Assess Substances in Blood or Urine:
Tests to Assess Monoclonal Protein

• **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
Bone Marrow Tests

- Complete Blood Count (CBC)
- Creatinine Clearance
- BUN
- Serum Creatinine
- eGFR
- Sβ2M
- LDH
- CRP
- SPEP/UPEP
- Total Protein
- Glucose
- QIg
- Freelite
- Hevylite
- Bone marrow biopsy
- Flow cytometry
- Cytogenetics
- Tests to assess blood cells
- Tests to assess kidney function
- Tests to assess blood proteins, etc
- Tests to assess monoclonal protein
- Tests to assess bone marrow
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
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
• **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

- Complete Blood Count (CBC)
- Creatinine Clearance
- Creatinine
- Calcium
- Protein
- Sβ2M
- LDH
- Total protein
- Glucose
- SPEP/UPEP
- Qlg
- CRP
- Flow cytometry
- Freelite
- Hevylite
- Bone marrow biopsy
- Bone marrow biopsy
- Cytogenetics
- PET
- CT
- X-ray
- MRI

Tests to assess:
- Blood cells
- Kidney function
- Blood proteins, etc
- Monoclonal protein
- Bone marrow
- Bone/areas outside bone
• 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
• MRI (Magnetic Resonance Imaging)
  – Uses magnetic energy, not radiation
  – Highly sensitive for detection of early bone marrow 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 (although CT does not use gadolinium)
Imaging Studies

• **PET (Positron Emission Tomography)**
  – Whole-body, real-time study
  – Shows where cancer is actively growing in the body
  – Used when patient has non-secreting 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
Imaging Tests

- Complete Blood Count (CBC)
- Creatinine Clearance
- BUN
- Freelite
- Hevylite
- Cytogenetics
- Serum Creatinine
- S\textsuperscript{β}2M
- CRP
- Q\textsubscript{lg}
- Bone marrow biopsy
- Flow cytometry
- PET
- eGFR
- LDH
- SPEP/UPEP
- IFE
- Flow cytometry
- CT
- FiSH
- X-ray
- MRI
- Calcium
- Total protein
- Glucose
- X-ray
- MRI
- Tests to assess blood cells
- Tests to assess kidney function
- Tests to assess blood proteins, etc
- Tests to assess monoclonal protein
- Tests to assess bone marrow
- Tests to assess bone/areas outside bone
Resources for More Info

• IMF's *Understanding Your Test Results* and *Understanding Freelite and Hevylite Tests*, available on the IMF website’s at [www.myeloma.org/imf-publications/understanding-series](http://www.myeloma.org/imf-publications/understanding-series) or call the IMF for a hard copy at 800-452-2873

• An IMF video on protecting yourself and your medical information in the age of electronic medical records (EMR) is available on YouTube at [https://youtu.be/GkAxSlT9tuc](https://youtu.be/GkAxSlT9tuc). Our EMR tip card is on our website at [https://www.myeloma.org/tc-emr](https://www.myeloma.org/tc-emr)

• For more information on the BSRI-funded NGF test for MRD testing, go to [https://www.myeloma.org/research/bsri](https://www.myeloma.org/research/bsri)