The Truth about Serum Proteins

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AAIM Webinar
Outline

- Serum proteins-constituents
- Albumin
- Low albumin levels
- Globulins
- Low globulin levels
- Elevated globulin levels
- Plasma cell dyscrasias-focus on MGUS and light chain disease
- Summary-key points
Normal Serum Proteins

- **Total proteins** = albumin + globulins
- **Total proteins** – albumin = globulins

- **Globulins** = alpha 1 + alpha 2 + beta + gamma globulins
**Albumin**

- Most abundant plasma protein-50-60 % of plasma proteins; women have albumin levels that are lower than men’s levels
- **Albumin** gene is located on 4q11-q13; synthesized exclusively in the liver; 12-15 grams per day; half life ~ 3 weeks
- **Albumin** functions:
  - a) **carrier protein**-bilirubin, calcium copper, thyroid hormone, fatty acids, drugs (which prevents drugs from being filtered by the kidneys), and many other compounds
  - b) provides >75% of colloid **oncotic pressure** a physiochemical force to keep water in blood vessels
  - c) **antioxidant** by providing the largest source of thiol, which binds nitric oxide
Albumin Molecule Diagram
Elevated Albumin

- For underwriting purposes, there are no diseases or problems associated with an elevated albumin. However, albumin can be elevated if there is significant dehydration or volume depletion.
Low Albumin-Hypoalbuminemia

- A low albumin is associated with an increased mortality risk. Patients with albumin <3.5 gm% at 3 months after discharge from hospital have a 2.6x increased 5 year mortality than those with a serum albumin >4.0 gm%.

- Causes of low albumin include:
  - Poor diet - a 24 hour fast decreases albumin synthesis by one third
  - Protein losing enteropathies - colitis, enteritis, sprue
  - Liver diseases - severe acute hepatitis, cirrhosis
  - Renal diseases with proteinuria - nephrotic syndrome
  - Pregnancy
  - Acute or chronic infections, autoimmune diseases
  - Various malignancies
Hypoalbuminemia Study #1

Albumin Levels Predict Survival in Patients With Systolic Heart Failure

• Hypoalbuminemia is common in heart failure (HF) and is independently associated with increased risk of death in HF. Our analysis demonstrates a significant correlation of high-sensitivity C-reactive protein to low albumin levels, suggesting that inflammation may be an underlying etiology of hypoalbuminemia in HF. Furthermore, patients with hypoalbuminemia in this cohort were more likely to have low cholesterol levels and anemia, additional conditions that may be associated with inflammation in HF.

Hypoalbuminemia Study #2

Is Serum Albumin an Independent Predictor of Survival in Ovarian Cancer?

• Univariate and multivariate survival analysis found that low levels of serum albumin adversely affected survival by a statistically significant level across all stages of ovarian cancer independent of stage at diagnosis, serum cancer antigen-125, and previous treatment history. Patients with serum albumin scores of $\geq 3.6$ g/dL had a statistically significantly better survival than those with scores $\leq 3.5$ g/dL independent of stage at diagnosis and previous treatment history.

• D. Gupta; C. A. Lammersfeld; P. G. Vashi; S. Dahlk; J. F. Grutsch; C. G. Lis: Clin Ovarian Cancer. 2009;2(1):52-56. © 2009 CIG Media Group, LP
Hypoalbuminemia in Acute Illness: Is There a Rationale for Intervention?

• A meta-analysis was conducted of 90 cohort studies with 291,433 total patients evaluating hypoalbuminemia as an outcome predictor by multivariate analysis and, separately, of nine prospective controlled trials with 535 total patients on correcting hypoalbuminemia.

• Hypoalbuminemia is strongly associated with poor clinical outcomes.

• J-L. Vincent, MD, PhD, FCCM, M-J. Dubois, MD, R. J. Navickis, PhD, M. M. Wilkes, PhD: *Annals of Surgery*. 2003;237(3) © 2003 Lippincott Williams & Wilkins
Hypoalbuminemia Study #4

Albumin and All-Cause Mortality Risk in Insurance Applicants

• 1,704,566 insurance applicants with 53,211 deaths per Social Security Death Master File, median follow-up of twelve years, were stratified by age, sex, and albumin levels.

• **Conclusion:** When stratified by age and sex, low albumin discriminates between all-cause mortality risks in healthy adults at all ages and across a wide range of values independent of other laboratory tests.

• Fulks M, Stout RL, Dolan VF: *J Insur Med* 2010;42:11-17
Hypoalbuminemia Study #4

- Six groups by age and gender were studied using ages 20-49, 50-69, 70 and older, male and female

- Only exclusion criteria:
  - urine protein/creatinine ratio > 1g/g
  - found only in 0.2% of applicants

- Second look exclusions:
  - cholesterol <160 mg/dL
  - elevated AST, ALT, alkaline phosphatase
  - had little impact on relative risk except at the lowest 0.5% of albumin values
Hypoalbuminemia Study #4

- At thresholds of ~3.8 mg/dL albumin, the relative mortality risk exceeded 150% for all female age groups and males 70 and older.

- For males 20-69, the relative mortality risk exceeded 150% at albumin=4.1 mg/dL.

- Increasingly lower albumin levels were associated with increasing mortality risk, except in younger females, perhaps related to dilutional hypoalbuminemia of pregnancy.
### Hypoalbuminemia Study #4

#### Males 50-69

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Mortality Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4.3</td>
<td>100%</td>
</tr>
<tr>
<td>4.1-4.3</td>
<td>135%</td>
</tr>
<tr>
<td><strong>4.0-4.1</strong></td>
<td><strong>153%</strong></td>
</tr>
<tr>
<td>3.9-4.0</td>
<td>182%</td>
</tr>
<tr>
<td>3.75-3.9</td>
<td>221%</td>
</tr>
<tr>
<td>3.65-3.75</td>
<td>280%</td>
</tr>
<tr>
<td>&lt;3.65</td>
<td>407%</td>
</tr>
</tbody>
</table>

#### Females 50-69

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Mortality Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4.1</td>
<td>100%</td>
</tr>
<tr>
<td>3.95-4.1</td>
<td>113%</td>
</tr>
<tr>
<td>3.85-3.95</td>
<td>141%</td>
</tr>
<tr>
<td><strong>3.75-3.85</strong></td>
<td><strong>154%</strong></td>
</tr>
<tr>
<td>3.65-3.75</td>
<td>172%</td>
</tr>
<tr>
<td>3.5-3.65</td>
<td>209%</td>
</tr>
<tr>
<td>&lt;3.5</td>
<td>309%</td>
</tr>
</tbody>
</table>
Globulins

- **Globulins** are a group of proteins found in blood that are insoluble in water, but dissolve in a saline solution. There are many different, unrelated globulins. They have many different and diverse functions.

- **Globulins** are arbitrarily separated into alpha, beta and gamma regions depending on where the globulins migrate in an electromagnetic field. **Albumin** is the most negatively charged protein, followed by the **globulins**-alpha, beta, gamma, in that order.
Globulins

- Alpha-1 globulins
  - alpha-1-antitrypsin
  - alpha-1-antichymotrypsin
  - orosomucoid (acid glycoprotein)
  - serum amyloid A
  - alpha-1-lipoprotein (HDL)
Globulins

- **Alpha-2-globulins**
  - alpha-2-macroglobulin (protease inhibitor)
  - haptoglobin (binds free Hgb)
  - protein C (anti-coagulation factor)
  - angiotensinogen
  - ceruloplasmin (carries six copper molecules)
  - alpha-2-lipoprotein (VLDL)
  - thyroxine binding globulin
Globulins

- **Beta-1-globulins**
  - transferrin

- **Beta-2-globulins**
  - complement-C3, C4
  - CRP-C reactive protein (CRP)
  - plasminogen, fibrinogen
  - beta-2-microglobulin
  - beta-2-lipoprotein (LDL)
  - some IgA, IgM migrate in this region
Globulins

- **Gamma globulins**
  - IgA
  - IgD
  - IgE
  - IgG
  - IgM
Gamma Globulins

- **Gamma globulins**, also called **immunoglobulins**, are specific antibodies produced by specialized B lymphocytes called plasma cells.

- There are five types of **gamma globulins**—IgA, IgD, IgE, IgG, and IgM, produced by the plasma cells.

- The primary function of the plasma cells is to produce **gamma globulins**, which are also called **antibodies**. Each plasma cell produces only one antibody that is specific for one antigen.
Gamma Globulins

- The primary function of an antibody is to bind to a specific antigen, leading to the removal or inactivation of the antigen. The antigen may be a protein, toxin, virus, bacteria, parasite, fungus, medication, other foreign substances, or part of one’s own proteins (auto-antibodies).

- All five classes of gamma globulins have a similar structure, with two heavy chains and two light chains linked together. The five types of heavy chains are A, D, E, G, and M. The two types of light chains are kappa and lambda. Light chains are synthesized in slight excess of the heavy chains, but <10 mg/dl per day appear in the urine.
## Properties of Gamma Globulins

<table>
<thead>
<tr>
<th>property</th>
<th>IgG</th>
<th>IgA</th>
<th>IgM</th>
<th>IgD</th>
<th>IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>molecule and subclasses</td>
<td>monomer</td>
<td>dimer</td>
<td>pentamer</td>
<td>monomer</td>
<td>monomer</td>
</tr>
<tr>
<td></td>
<td>G1, G2, G3, G4</td>
<td>A1, A2</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>% of total serum Ig</td>
<td>80%</td>
<td>11%</td>
<td>8%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>level ranges</td>
<td>700-1700 mg/dL</td>
<td>70-350 mg/dL</td>
<td>50-300 mg/dL</td>
<td>0-14 mg/dL</td>
<td>10-179 mg/dL</td>
</tr>
<tr>
<td>biologic properties</td>
<td>placental transfer</td>
<td>secretory Ig</td>
<td>primary antibody</td>
<td>marker for mature B-</td>
<td>allergy</td>
</tr>
<tr>
<td></td>
<td>secondary antibody</td>
<td></td>
<td>response</td>
<td>cells</td>
<td>antiparasite</td>
</tr>
<tr>
<td></td>
<td>response</td>
<td></td>
<td></td>
<td></td>
<td>responses</td>
</tr>
<tr>
<td>half life</td>
<td>23 days</td>
<td>6 days</td>
<td>5 days</td>
<td>3 days</td>
<td>2.5 days</td>
</tr>
</tbody>
</table>
Low Gamma Globulins

- A low globulin level is called **hypoglobulinemia** and is usually due to decreased gamma globulins, and thus, can also be called **hypogammaglobulinemia**.

- If the globulin levels are <1.8-2.0 gm%, one must be on the alert for a possible immunodeficiency, looking for fevers, chills, sweats, frequent infections, weight loss, plasma cell dyscrasias, lymphoproliferative disorders, etc.

- Dr. Winsemius of Heritage Labs has studied mortality risk of various globulin levels in relation to the serum albumin levels.
Low Gamma Globulins
# Low Gamma Globulins

## Albumin level/globulin level/mortality ratio

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Globulin</th>
<th>1.00-1.50</th>
<th>1.50-1.75</th>
<th>1.75-2.00</th>
<th>2.00-2.20</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0-3.5</td>
<td></td>
<td>-</td>
<td>873%</td>
<td>866%</td>
<td>333%</td>
</tr>
<tr>
<td>3.5-4.0</td>
<td></td>
<td>328%</td>
<td>354%</td>
<td>297%</td>
<td>150%</td>
</tr>
<tr>
<td>4.0-4.5</td>
<td></td>
<td></td>
<td></td>
<td>114%</td>
<td>97%</td>
</tr>
<tr>
<td>4.5-5.0</td>
<td></td>
<td>218%</td>
<td>76%</td>
<td>84%</td>
<td>71%</td>
</tr>
</tbody>
</table>

**Note:** With albumin levels 4.0 or greater, the globulins can dip to 1.5 before there is an appreciable increase in mortality risk.

**Note:** Higher albumin levels are associated with a more favorable mortality risk.
Elevated Gamma Globulins

- An elevated globulin level is called **hyperglobulinemia**. Since the elevation is usually due to elevated gamma globulins, the condition can also be called **hypergammaglobulinemia**.

- **Hypergammaglobulinemia** is only one of two types, either a **polyclonal** or a **monoclonal** increase of the gamma globulins. A serum protein electrophoresis (quantitative test) is the laboratory test that separates the two conditions.

- A **polyclonal** increase in gamma globulins is due to a reactive or inflammatory process. The concern for underwriting is the underlying disease causing the **polyclonal** increase in the gamma globulins. Though an increase in the globulins implies active disease, there are no additional concerns regarding the elevated globulin level per se.
Elevated Gamma Globulins

- Dr. Winseminius has also studied albumin and elevated globulin levels in relation to mortality risk. He found the following:

<table>
<thead>
<tr>
<th>Albumin level</th>
<th>globulin level</th>
<th>3.20-3.40</th>
<th>3.40-3.60</th>
<th>3.60-3.80</th>
<th>3.80-4.00</th>
<th>4.00-4.20</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5-4.0</td>
<td>189%</td>
<td>205%</td>
<td>262%</td>
<td>308%</td>
<td>494%</td>
<td></td>
</tr>
<tr>
<td>4.0-4.5</td>
<td>115%</td>
<td>134%</td>
<td>148%</td>
<td>199%</td>
<td>267%</td>
<td></td>
</tr>
<tr>
<td>4.5-5.0</td>
<td>96%</td>
<td>115%</td>
<td>123%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** With lower albumin levels, increasing globulin levels are associated with an increased mortality risk-unable to separate polyclonal or monoclonal increase.

**Note:** With albumin levels >4.0, globulin levels >3.8 are associated with an increased mortality risk-unable to separate polyclonal or monoclonal increase.
Polyclonal Elevated Gamma Globulins

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Elevated Gamma Globulins

- A **monoclonal** increase in gamma globulins is due to a malignant or potentially malignant clone of plasma cells producing a monoclonal antibody autonomously.

- A serum **immunoelectrophoresis** (qualitative test) determines the type of abnormal monoclonal protein produced.

- **Monoclonal** diseases are called **plasma cell dyscrasias**, plasma cell disorders or monoclonal gammopathies. The plasma cell disorders are all related disorders because the abnormal plasma cells develop from common progenitors in the B lymphocyte cell line.
Monoclonal Elevated Gamma Globulins

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**Monoclonal Elevated Gamma Globulins**

- **A.** Distribution of Monoclonal Proteins in 1485 Patients seen at the Mayo Clinic in 2008

- **B.** Diagnoses in 1626 patients with Monoclonal Gammopathy seen at the Mayo Clinic in 2008

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>56%</td>
<td>MGUS 56%</td>
</tr>
<tr>
<td>IgM</td>
<td>18.5%</td>
<td>Multiple Myeloma 21%</td>
</tr>
<tr>
<td>IgA</td>
<td>11%</td>
<td>Amyloidosis 11%</td>
</tr>
<tr>
<td>Biclonal</td>
<td>8%</td>
<td>Lymphoproliferative 4%</td>
</tr>
<tr>
<td>Light chain only</td>
<td>6%</td>
<td>Waldenstrom’s 2%</td>
</tr>
<tr>
<td>IgD</td>
<td>0.5%</td>
<td>other 6%</td>
</tr>
</tbody>
</table>
Plasma Cell Dyscrasias

1. Monoclonal Gammopathy of Unknown Significance- **MGUS**
2. Multiple Myeloma- **MM**
3. Waldenstrom’s Macroglobulinemia- **WM**
4. Heavy Chain Disease: gamma **HCD** (Franklin’s Disease)
   alpha **HCD** (Seligmann’s Disease)
   mu **HCD**
5. Primary amyloidosis- **AL**
6. Light chain disease- **LCD**
   - The plasma cell disorders are all considered as malignant or pre-malignant conditions. With the exception of monoclonal gammopathy of unknown significance-MGUS, the plasma cell disorders are associated with a very high mortality risk.
MGUS

- **MGUS** is the most common plasma cell disorder. The cause is unknown.
- **MGUS** is more common in males, 2x more common in blacks, and the prevalence increases with age:

<table>
<thead>
<tr>
<th>age</th>
<th>% of pop with MGUS</th>
<th>% males</th>
<th>% females</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>1.7%</td>
<td>2.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>60-69</td>
<td>3.0%</td>
<td>3.7%</td>
<td>2.3%</td>
</tr>
<tr>
<td>70-79</td>
<td>4.6%</td>
<td>5.6%</td>
<td>3.8%</td>
</tr>
<tr>
<td>80-85</td>
<td>6.6%</td>
<td>8.3%</td>
<td>6.0%</td>
</tr>
<tr>
<td>&gt;85</td>
<td>7.5%</td>
<td>8.9%</td>
<td>7.0%</td>
</tr>
</tbody>
</table>

**MGUS**

- The **M (M=monoclonal) component** or **M spike** is another name for the monoclonal protein found in **MGUS** and other plasma cell disorders.
- The diagnosis of **MGUS** includes:
  a. M component <3 gm/dL
  b. Bone marrow plasma cells <10%
  c. Small amounts or no Bence-Jones proteinuria
  d. No lytic bone lesions, anemia, renal failure, hypercalcemia
MGUS

- **MGUS M component** heavy and light chain characteristics:
  - IgG-69%
  - IgM-17%
  - IgA-11%
  - biclonal-3%
  - kappa-62%; lambda-38%

- **M component** level
  - <1.0 gm/dL 63.5%
  - 1.0-2.0 gm/dL 32.0%
  - >2.0 gm/dL 4.5%
40% of MGUS patients have decreased normal gamma globulins (a relative hypogammaglobulinemia), causing an increased risk of bacterial infections (immunodeficiency).

Once diagnosed, MGUS patients should have a yearly serum protein electrophoresis (ELP) to monitor the M component level stability.
MGUS

- Non-plasma cell disorders associated with a monoclonal gammopathy: Non-Hodgkin's lymphomas B cell types, CLL-chronic lymphatic leukemia, hairy cell leukemia, mycosis fungoides, chronic liver disease, Gaucher’s disease, pyoderma gangrenosum, post-liver, -kidney, -bone marrow, or -heart transplants, 5% of peripheral neuropathy cases

- There is a risk of progression from MGUS to a malignant plasma cell disorder (most commonly multiple myeloma) that persists lifelong, approximately 1% malignant transformation risk per year.
There are three risk factors for malignant progression:

1) **IgG**-lower risk; **IgM, IgA** higher risk; bone marrow plasma cells < 5%

2) **M component** < 1.5 gm/dL lower risk; > 1.5 gm/dL higher risk

3) **abnormal FLC** (free light chain ratio) **kappa/lambda**, normal = 0.26-1.65

### Risk  Absolute progression risk 20 yrs   # Patients

- low  5%  449
- 1 risk factor  21%  420
- 2 risk factors  37%  226
- 3 risk factors  58%  53
MGUS Mortality Risk

The results of a Danish study by Gregerson, et al, found the following mortality data in 1,324 cases of MGUS:

- 868 deaths, 410 expected deaths  \( \text{SMR}=2.1 \)
- 97 malignant plasma cell disorders
- 5 expected transformations  \( \text{SMR}=20 \)

- *British Journal of Hematology, 2001*
Light Chain Disease

- **Light chains** are synthesized by plasma cells in slight excess of heavy chains, with which the light chains assemble to form immunoglobulins or antibodies.

- The excess **light chains** are filtered in the glomerulus, reabsorbed by the proximal tubular kidney cells, and catabolized by lysosomal enzymes in the proximal tubule cells. Only a small amount of light chains normally appear in the urine.

- **Bence-Jones protein** in the urine is excess homogeneous light chains, either kappa or lambda, and is presumed to be the product of a single clone of plasma cells.
Light Chain Disease

- **Lambda** light chains are more toxic to the renal tubules than **kappa** light chains and are associated with a worse prognosis.

- In adults, **light chain disease** or **Bence-Jones proteinuria** is usually related to plasma cell dyscrasias, more common in males, occurs in all racial groups, and the onset is about age 53.

- **Light chain** MGUS-analogous to MGUS with progression to end-organ damage and plasma cell malignancy
**Light Chain Disease**

- Diseases associated with **light chain disease**:
  - **Frequent:**
    - **Multiple Myeloma** ~47-70% of cases
      - IgG myeloma-60%, kappa light chains
      - IgA myeloma-71%, kappa light chains
      - IgM myeloma-100%, lambda light chains
    - **Waldenstrom’s macroglobulinemia** ~35% of cases
    - **Amyloidosis** ~92% of cases, lambda light chains
  - **Less frequent:**
    - Non-Hodgkins lymphoma, CLL-chronic lymphatic leukemia
Multiple Myeloma

- The diagnosis of **Multiple Myeloma** includes:
  a. >10% plasma cells in the bone marrow
  b. Monoclonal immunoglobulin, usually >3 gm/dL
  c. Lytic bone lesions
  d. Susceptibility to bacterial infections
  e. Anemia
  f. Renal failure-light chain nephropathy, hypercalcemia
  g. Hypercalcemia due to destruction of bone
Multiple Myeloma

- Types of monoclonal proteins found in **multiple myeloma**:
  - IgG 52%
  - IgA 21%
  - Bence-Jones Proteinuria 16%-kappa-65%, lambda 35%
  - Non-secretory-no M protein 3%
  - IgD 2%
  - Biclonal 2%

Overt myeloma occurs in nearly 50% of **solitary plasmacytoma** cases within 3 years.
## Plasma Cell Dyscrasias

<table>
<thead>
<tr>
<th>Item</th>
<th>Multiple myeloma</th>
<th>Waldenstrom's Macroglobulinemia</th>
<th>Heavy Chain Disease</th>
<th>Primary Amyloidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>unknown</td>
<td>unknown</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td><strong>Median age at dx</strong></td>
<td>65</td>
<td>65</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td><strong>Sex incidence</strong></td>
<td>male &gt; female</td>
<td>male(60%) &gt; female</td>
<td>male(60%) &gt; female</td>
<td>male ~ female</td>
</tr>
<tr>
<td><strong>Racial incidence</strong></td>
<td>2xB:W &gt; A</td>
<td>W &gt; B</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cases per year</strong></td>
<td>14,000</td>
<td>1500</td>
<td>&lt;500 cases published</td>
<td></td>
</tr>
<tr>
<td><strong>Gammopathy type</strong></td>
<td>IgG-52%, IgA-21%, light chains-16%</td>
<td>IgM</td>
<td>truncated</td>
<td>light chains</td>
</tr>
<tr>
<td><strong>Median survival</strong></td>
<td>4-6 years</td>
<td>6 years</td>
<td>&lt;5 years</td>
<td>18 months</td>
</tr>
</tbody>
</table>
**Key Points**

- **Low albumin** is associated with an increased mortality risk. There is evidence that levels <3.8 g/dL in females and <4.0 g/dL in males are associated with some increased mortality risk.

- **Low globulins** are associated with an increased mortality related to possible immunodeficiency. There is evidence that if albumin is >4.0 g/dL, globulins can dip to 1.5 g/dL before the mortality risk rises.

- **Elevated globulins** are associated with an increased mortality risk, especially if globulins are >3.8 g/dL and if the albumin is low.
Key Points

- **Elevated globulins** can be due to polyclonal or monoclonal gammopathies. **Polyclonal** gammopathies are rated for the disease causing the increased globulins.

- **Monoclonal** gammopathies are usually due to plasma cell dyscrasias.

- Except for **MGUS**, the plasma cell dyscrasias have very poor median survivals, ≤6 years.

- The three factors for increased risk of **MGUS** progression to a more serious plasma cell dyscrasia are given (slide 38).

- **Light chain disease** must be carefully underwritten, looking for the possibility of a serious plasma cell dyscrasia.
References

2. Parmar MS: Light-Chain Associated Renal Disorders. Medscape article 244082, 21 Aug 2008