

Prostatic Acid Phosphatase : A Test Who's Time Is Done



For the diagnosis and monitoring of prostate cancer the literature now provides excellent documentation of the superior sensitivity and specificity of serum prostate specific antigen (PSA) measurement compared to prostatic acid phosphatase (PAP).

Diagnosis and Staging

PAP does not demonstrate adequate sensitivity in early stage disease (Table 1)

and is subject to analytical and physiological interferences related to the timing of specimen collection after digital rectal examination (DRE) and sample hemolysis. In rare cases, however, PAP is important in the diagnosis of non-PSA secreting prostatic tumors.

Measurement of serum PSA offers enhanced sensitivity in early stage (A and B) disease allowing early diagnosis and treatment although false positive PSA results may be generated in patients with benign prostate hypertrophy (BPH). In metastatic disease, measurement of PSA identifies the need to perform bone scans. Reports describing the biological variability indicate that PSA is more stable when compared to PAP.

Table 1: Clinical Sensitivity of PSA and PAP (%)

Disease Stage	PSA	PAP
A	67	11
B	73	22
C	80	39
D	88	58

Monitoring

After a course of therapy, low serum total PSA concentrations support a very good prognosis and documents absence of residual disease. Since PAP is released from tissues other than the prostate, the level of blood PAP does not reflect the success of therapy and the need for further interventions.

Summary

The recommended laboratory test for diagnosing, staging and monitoring of prostate cancer is serum total PSA. Assay of free PSA is helpful when the total PSA is between 4-10 µg/L. Routine measurement of PAP is not suggested.

References

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Nasal Cultures: The Value of Microbiological Testing

The anterior nares of healthy individuals will often harbour a wide variety of organisms including *Staphylococcus aureus*, *Haemophilus influenzae*, *Neisseria* species, and streptococcal species. While some of these agents are known to cause both upper and lower respiratory tract infections, their recovery from a nose swab is not predictive of an etiologic role.¹

The recovery of *Staphylococcus aureus* from the anterior nares, however, may indicate carriage of the organism, or "colonization" which may be associated with subsequent staphylococcal infection.² Staphylococcal colonization has also been associated with spread of the organism within hospitals and other institutional settings.

Accordingly, all nose swabs (preferably from the anterior nares) will be routinely assessed in the laboratory for the presence of *Staphylococcus aureus* only. All staphylococcal isolates are screened for resistance to beta-lactam antibiotics (MRSA).

The nasopharyngeal swab is the specimen of choice when investigating suspected cases of pertussis or viral respiratory tract infection (i.e. influenza). These specimens should be delivered to the laboratory in the specific transport media supplied by the Public Health Laboratory. Alternatively, nasopharyngeal washings may be submitted for such investigations.

References

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In This Issue

Prostatic Acid Phosphatase :
A Test Who's Time Is Done 1

Nasal Cultures: The Value of
Microbiological Testing 1

Clinical and Laboratory Evaluation
of Monoclonal Gammopathies . . . 2

Lab Notes

Serum Allergy Testing
Available at MDS 3

Pap Smears 3

Clinical and Laboratory Evaluation of Monoclonal Gammopathies

Overview

The monoclonal gammopathies represent a group of disorders that result from over-production of a single homogeneous immunoglobulin due to an abnormal clone of plasma cell precursors of the B-cell lineage. They may be plasmacytic, lymphocytic, protein infiltrative or a miscellaneous disorder. Increased numbers of plasma cells are present in the bone marrow and there is an increased concentration of a specific immunoglobulin in the serum or urine that produces a significant, discrete band on an electrophoresis gel.

Accurate diagnosis is based on bone marrow histomorphology and radiological studies as well as specific serum chemistry findings.

Clinical presentation

Individuals with a monoclonal gammopathy may present with mixed clinical features including severe bone pain, nausea, anemia, fatigue, confusion, blurred vision and skin nodules. Osteoporosis, renal insufficiency and hypercalcemia are other features that may complicate the patient's clinical status.¹ The most prevalent cause of plasma cell dyscrasia is multiple myeloma.²

It is important to note that approximately 3% of patients over the age of 70 may have a monoclonal gammopathy but are asymptomatic and present with stable biochemical markers. Such cases are referred to as 'monoclonal gammopathy of undetermined significance' (MGUS) and typically present with IgG concentrations of <20 g/L and/or IgA < 10 g/L.^{3,5} Studies have shown that fifteen percent (15%) of these patients may develop a malignant plasma cell dyscrasia disorder within 10 years.

Unfortunately, there are no laboratory studies that reliably predict which MGUS patients will progress to multiple myeloma.

Other rare types of monoclonal gammopathies include heavy chain disease, Waldenstrom macroglobulinemia, solitary plasmacytoma, amyloidosis and immunoglobulin disposition disease.

Diagnosis and Monitoring of a Monoclonal Gammopathy

Identification

Serum protein electrophoresis is indicated in all patients with suspected plasma dyscrasia.²

Electrophoresis gels are examined in the laboratory by densitometry and also visually to identify weak protein bands not detected by densitometry. The report generated indicates the presence or absence of significant abnormal protein fractions and recommendations for follow-up testing of the abnormal M-protein (monoclonal or paraprotein) fraction.

It is recommended that all patients with a monoclonal gammopathy be assessed for the level and type of free light chains excreted using a 24-hour urine collection.²

To secure the diagnosis, there should be documentation of at least one of the major and one of the minor criteria listed in Table 1.

Table 1. Criteria for the Diagnosis of Multiple Myeloma⁶

Major Criteria

- Plasmacytoma
- Bone marrow > 30% plasma cells
- Presence of a monoclonal protein fraction on serum electrophoresis with > 35 g/L (IgG) or > 20 g/L (IgA) or > 1g/day urine free light-chain excretion.

Minor Criteria

- Bone marrow plasmacytosis > 10%
- Presence of a monoclonal protein fraction on serum or urine electrophoresis but less than the levels listed in the major criteria.
- Decreased concentration of residual, uninvolved immunoglobulins
- Lytic bone lesions

Upon detection of an abnormal protein fraction, identification of the nature of the protein by immunofixation is indicated. Using protein immunofixation technology the heavy and light chain components are characterized and the presence of free light or free heavy chains is determined.

Historical data indicates that about 60% of cases are IgG type and 20% are IgA type.⁶ When only light chains appear in the serum and/or urine and a positive Bence Jones protein is detected in urine, a diagnosis of light chain disease is confirmed. Prevalence of light chain disorder is close to 20%. Heavy chain disorders are rare.

(continued on page 4)

Serum Allergy Testing Available at MDS

MDS now offering testing for in vitro diagnosis of IgE mediated hypersensitivity reactions using the Pharmacia ImmunoCAP™ system. This system detects IgE antibodies directed against specific allergens and has greater sensitivity and specificity than earlier serological methods e.g. the RAST test.

After a detailed clinical history is obtained, clinicians may choose to proceed to skin prick testing or serologic testing to confirm diagnosis of an allergy. The later may be particularly valuable with young patients, individuals with atopic dermatitis and those who have been receiving long-acting antihistamines.

Serologic testing may be ordered by completing the MDS Allergen request form that lists readily available single and "mixed" allergens. Other allergens are also available upon request. Since over 450 allergens can be evaluated, it is recommended that initial investigations target a suspected panel ("mix") of allergens followed by more selective allergen choices based upon the initial result(s).

For more information on allergy testing, please telephone us a 416-675-3637. Clinical information is also available at the Pharmacia supported web site www.isitallergy.com. These tests are not covered by OHIP but may be included in some family insurance plans.

Pap Smears

Most gynecological cytology samples submitted to MDS are from healthy women participating in the Cervical Cancer Screening Programme. These specimens are screened by cytotechnologists and if adequate and apparently normal are reported. Targeted re-screening of high-risk smears is undertaken under the following circumstances.

- When there is history of a previous abnormal smear.
- When clinical information is provided by you, which places your patient in a high-risk group. MDS regards the following information to place the patient in high-risk categories for targeted re-screening purposes are as follows:


Description of Cervix:	Abnormal Bleeding:
Erosion	Postmenopausal bleeding
Visible Lesion	Contact bleeding
Friable Cervix	Post-coital bleeding
Abnormal Cervix	Abnormal bleeding (not specified)

History of:

- Herpes
- DES exposure
- ASCUS/AGUS
- Dysplasia
- Family History of Carcinoma (not specified)
- Cervical Carcinoma
- Endocervical Carcinoma
- Endometrial Carcinoma (not to include vault smears)
- Biopsy
- Cryotherapy
- Laser therapy
- LEEP/LOOP
- Irradiation therapy

It is important to include pertinent information on the laboratory requisition otherwise your patient will be considered to be a healthy female with no characteristics placing her in the high-risk group for targeted re-screening.

Targeted and random re-screening is carried out to minimize the chance of a false negative Pap Smear. Equally important in this regard is participation of women in the screening program at regular intervals. There is an information sheet behind the MDS cytology requisition, which you may give to your patients reminding them of this.

When new requisitions are printed this information will appear on the front page and two boxes will be added which enable you to remind the patient to return for a repeat Pap Smear in one or two years depending on previous history of participation in the program unless of course an abnormal report requires intervention prior to the regular screening interval. 



"Targeted re-screening of PAP smears is automatically undertaken as a result of an abnormal PAP history or clinical symptoms. Please be sure to include all pertinent information on the laboratory requisition."

(continued from page 2)

It is not necessary to repeat serum immunofixation analysis unless there is a change in the electrophoretic pattern such as a shift in the position of the immunoglobulin peak or the development of a new protein fraction.² In patients with known disease, however, a physician may wish to confirm remission post-therapy.


Immunofixation is not indicated in patients with an obvious polyclonal gammopathy.²

Monitoring

Disease progression may be monitored through quantitative measurement of the specific protein classes identified from the immunofixation analysis (IgG, IgA, IgM).² At diagnosis, it is important to assess the concentration of total residual immunoglobulins by immunoglobulin quantitation, but this should not be used as a means of screening patients suspected of having a monoclonal gammopathy. In classical multiple myeloma, the M-protein is abnormally increased in concentration; concentrations of the other immunoglobulin classes are typically decreased.³ Changes to the patient's clinical status and protein profile may be monitored via densitometric estimation or quantitative determination of the immunoglobulins.

Quantitative measurement is more accurate than densitometric determination, particularly in cases where the concentration of immunoglobulin of the M-protein is low, as with IgA and IgM

monoclonal protein, or when the M-protein is obscured by other proteins. Densitometric estimation, while imprecise, has the advantage that it is less affected by the antigenic composition of the monoclonal peak compared to that used for method calibration. Estimation of the M-protein by densitometry is possible when it is present as a clearly defined fraction.

For patients with multiple myeloma, Waldenstrom disease or amyloidosis, serum and/or urine protein electrophoresis and quantitation of the specific protein(s) should be assessed at regular intervals. Patients with MGUS should be monitored at least annually for changes in their protein profile.² 

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