**INTRODUCTION**

An adrenal incidentaloma is an adrenal mass detected on a medical imaging examination done for indications other than adrenal disease.

**INVESTIGATIONS**

Once detected, a review of clinical history along with a clinical examination focusing on the signs and symptoms suggestive of adrenal hyperfunction or malignancy disease and hormonal testing to confirm the diagnosis is warranted.

3. Primary Adrenocortical: Approximately 1% of patients on work up have been proved to have Cushing’s Syndrome. Serum cortisol estimation is not a reliable screening modality. The ratio of ambulatory morning plasma cortisol concentration to plasma renin activity is a good screening test. If the ratio is high (>20), the diagnosis can be confirmed by an additional measurement of plasma aldosterone levels (>15ng/dl).

**RADIOLOGICAL INVESTIGATIONS**

A fine cut (3 mm) high resolution contrast enhanced CT scan is the gold standard for investigating adrenal masses. Adenomas are usually 2cm or less in size, solitary, unilateral and are round or oval with a distinct margin. On a non contrast CT, the attenuation is 10HU or less and with contrast, the lesion is not washout with a wash out of less than 50% in 10 minutes. Conversely, adenocortical carcinomas are usually greater than 4 cm in size and lack washout. The lesion on a plain CT scan is greater than 10 HU. The lesion is vascular and the washout of contrast medium is less than 50% in 10 minutes. Necrosis and hemorrhage is commonly seen.

**BIOPSY/ CYTOLOGY**

As the serum and urine testing for Cushing’s disease is not diagnostic, adrenalectomy is the investigation of choice. Invasive investigation by biopsy is not indicated in the work up of patients with incidentally detected adrenal masses except when metastasis in the adrenal gland is highly likely e.g. known history of previous cancer resected. If MRI is being considered then all efforts must be made to exclude phaeochromocytoma.

**MANAGEMENT AND FOLLOW UP**

An algorithm for the management of adrenal incidentaloma is shown in Figure 1. Measurement of fractionated metanephrines and catecholamines in the urine is the gold standard in these patients for whom an operation is warranted. While it is accepted that it is a safe operation with a mean post operative stay of two days and return to work in a week. The size limit for laparoscopic excision is being raised considerably with masses up to 10cm in size being safely removed laparoscopically. In those cases where the operation has been delayed, follow up is recommended with repeat CT scanning at 6, 12 and 24 months.

**PSA IS A GOOD TEST BUT NOT GOOD ENOUGH**

Over the years, there have been various concerns reporting the poor performance of PSA as a screening tool for prostate cancer. One criticism is the fact of there being a number of cancers that are missed where the test result has normal and in spite of digital rectal examination findings on the prostate being normal as well. Additionally, PSA has failed to separate those reasons other than prostate cancer and for many of these men, this leads to invasive investigation and associated anxiety. Thirdly, there are cancers that are diagnosed that are not of clinical significance and arguably did not need to be found in the first place. The drawbacks of PSA testing have stimulated research into the development of alternative tests to better assign patients who need a prostate biopsy.

PSA is most accurately referred to as being a diagnostic test for prostate cancer. Its role is in ascertaining which men are at sufficient risk of having prostate cancer to justify or avoid diagnostic testing in the form of a prostate biopsy. There has been publicity over a number of tests that have demonstrated some promise in being superior to PSA testing but most of these have ultimately failed to demonstrate superiority and have faded into oblivion. There are, however, two tests which are showing greater promise than any of their predecessors that could potentially be available for widespread usage within a few years.

**EARLY PROSTATE CANCER ANTIGEN (EPCA - 2) TESTING OF THE BLOOD**

The most promising blood test is the Early Prostate Cancer Antigen – 2 (EPCA - 2). The first study published last year 213 men were screened out of 11,120 participants. The Johns Hopkins published last year and the early data is suggesting that test performing significantly better than PSA at identifying individuals with prostate cancer. In their study published last year, 330 men were enrolled in the study according to the 6 groups and a control group as outlined in Table 1. An abnormal EPCA level was defined an abnormal EPCA level was defined abnormal - 2 level was >30ng/mL. In those men who were not picked up by the test, they are well defined according to whether there is prostate cancer present or not. The standard deviations in the few above study help illustrate the promising ability of the EPCA -2 to differentiate between subjects with and without prostate cancer. There is also some suggestion that this test is able to discriminate between organ confined disease and non organ confined disease (Table 1).

The overall specificity of the EPCA -2 in correctly identifying organ confined and non organ confined prostate cancer was 90% and 98% respectively. The sensitivity in the EPCA -2 in correctly identifying subjects without prostate cancer was 97% although for the BPH subgroup it was still impressive at 92%. In comparison, the sensitivity for PSA at a cut-off of 2.5ng/ml was 65% and specificity was 90%.

The real advantage in the EPCA -2 test appears to be its help in identifying those men without prostate cancer irrespective of their PSA level and the test could have a major impact on appropriately assigning patients to undergo prostate biopsy. The additional potential benefit may lie in the ability of the level of EPCA -2 to be able to sort men with likelihood organ confined and non-organ confined prostate cancer that if they were to undergo a radical prostatectomy. It is important to recognise that this was a pilot study and much larger numbers will be necessary to confirm the usefulness of this test but at this point in time there has not been any test that has shown as much potential as the EPCA -2 to replace PSA as the standard for early detection of prostate cancer.

**HUMAN CARCINOMA ANTIGEN (HCA) TESTING OF THE SEMEN**

Another test showing particular promise is a semen based test. Human carcinoma antigen (HCA) is a protein whose blood levels increase in association with most cancers. In normal prostate tissue it is expressed at high levels, but in prostate cancer it is expressed at low levels. As a result increased levels of HCA have been observed in both the blood and the ejaculate. Given that the finding of HCA in the blood is nonspecific for cancer type, its finding in the ejaculate at high levels is theoretically unlikely to be due to anything other than prostate cancer. The logical next step is to correlate findings of HCA in the semen with prostate biopsy results as well as comparing its performance to PSA blood testing. A small number of men have been enrolled in the first of such studies but a much larger scale study at the San Clinc has just commenced. Human Research Ethics Committees approval has recently been confirmed. Men who are about to undergo a prostate biopsy were invited to participate in this study were semen samples are also collected for analysis. From a practical viewpoint, it is unlikely that a semen based test that will on its own achieve complete acceptance as a replacement routine ‘screening’ test for PSA but will likely be an important adjunct to help clarify which abnormal PSA tests that require progression to biopsy. The test is more likely to achieve acceptance as a screening tool in higher risk individuals such as those with a strong family history of prostate cancer or prostatic individuals.

**REFERENCES**

Available upon request.

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**NEW DIAGNOSTIC TESTS FOR THE EARLY DETECTION OF PROSTATE CANCER?**

by Dr Henry Woo

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**APRIL/MAY 2008**

**MANAGEMENT OF ADRENAL INCIDENTALOMAS**

by A/Prof Stan Sidhu

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**Figure 1. An Algorithm for the Evaluation of Incidentally discovered Adrenal Mass.**

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**Table 1. EPCA -2 testing results**

<table>
<thead>
<tr>
<th>Control group</th>
<th>Clinical BPH with normal PSA (PSA&lt;2.5ng/mL)</th>
<th>Control group</th>
<th>Clinical BPH with normal PSA (PSA&lt;2.5ng/mL)</th>
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</thead>
<tbody>
<tr>
<td>PSA</td>
<td>EPCA</td>
<td>PSA</td>
<td>EPCA</td>
</tr>
<tr>
<td>n</td>
<td>Mean</td>
<td>n</td>
<td>Mean</td>
</tr>
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<tr>
<td>EPCA</td>
<td>2.53</td>
<td>Control group</td>
<td>3.03</td>
</tr>
</tbody>
</table>

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**ADVANCED MEDICINE**

by Dr Peter Fong

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**UROLOGICAL SURGEON**

by Dr Henry Woo

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**UROLOGICAL SURGEON**

by Dr Henry Woo

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**REFERENCES**

Available upon request.
MELANOMA
IN BRIEF - A FIVE MINUTE GUIDE TO MANAGEMENT

by Dr T. Michael D. Hughes

INTRODUCTION

Melanoma is a common cause of death for adults of all ages. Recent media campaigns have raised public awareness that has undoubtedly led to an increase in consultations related to melanoma. This article is a timely review of the management of melanoma that summarises many of the recommendations that will appear in the upcoming edition of Guidelines for the Management of Cutaneous Melanoma. Encouragingly, in spite of these awareness campaigns, melanoma, like other malignancies, remains a common cause of delay in diagnosis.

CLINICAL DIAGNOSIS

There is no doubt that melanoma awareness and early detection has contributed to good outcomes for most patients. Nevertheless, a significant number of patients are diagnosed with higher risk melanomas, either because of delayed presentation or because of delayed diagnosis.

The most important step is to consider the possibility of melanomas, but as melanomas have a wide spectrum of biological behaviour, the clinical presentation is quite varied. The clinician must be aware of these variations. Melanomas can arise from normal skin or from pre-existing moles. They do not have to be pigmented (5% - 10%). Some variants present as a small lump with normal appearing skin over the surface. Some are flat and others raised. They can arise in areas with minimal or no sun exposure. Flat or barely palpable macules are very commonly found on the face and limbs. These are usually caused by an excess of pigment in the skin (fleabite, solar lentig or pigment in other lesions such as blue naevi, BCCs) but can also be a prominent manifestation of melanocytic Pigmented Lentigines (PMEL). These can be widespread and often go undetected until a significant change occurs.

The key to a good outcome with melanoma is an early diagnosis. Early diagnosis can be achieved at any stage from inception to detection. Skin cancer registries now report melanoma to be one of the most “survivable” malignancies in NSW.

The key to a good outcome with melanoma is an early diagnosis. Early diagnosis can be achieved at any stage from inception to detection. Skin cancer registries now report melanoma to be one of the most “survivable” malignancies in NSW.

The advantage of such a portfolio is that it can be used to assist in the management of future patients.

The information provided by the pathologist in their report is vital in determining these risks and the advice given to patients in regard to prognosis and management.

A combination of the traditional descriptive report and asummary report is preferred. The summary should include the Breslow Thickness (this is the most important), the presence or absence of ulceration, the mitotic rate, the presence of melanomas to the margins and the presence or absence of other features such as lymphovascular invasion, neurotropism, desmoplasia or satellitosis. Most reports comment on evidence of regression. The depth of regression is not relevant to management. Clinical scores are always reported but have been shown to be unreliable.

MARGINS OF EXCISION

The concept is to remove the melanoma with a zone of normal skin that will contain any microscopic lateral extensions or any single cells that have separated from the main lesion. This is to minimise the risk of local recurrence which if it does happen may be at a greater depth than the original melanoma and therefore place the patient at greater risk of metastasis. Most wide excisions can be done with a simple ellipse and primary closure. Skin grafts and complicated flaps may be necessary on the distal excisions and the head but are rarely indicated elsewhere.

Compromise on margins can be made if it would simplify the procedure, reduce morbidity and avoid significant cosmetic or functional impact, but as long as patients are aware of the situation and will comply with regular follow-up.

BIOLOGY

Once suspected of being a melanoma, tissue should be obtained for histological examination. In most situations the suspect lesion should be excised completely with a narrow margin. The orientation of the excision should take into account the orientation of a later wider excision wound. In cases where complete excision would be a significant procedure (large lesions or lesions on the face/diabetic extremity), an incision biopsy taking ellipse is best. Precise biopsies can be used. Skin biopsy and squeezing should not be performed. Sampling error can occur with any incision biopsy. If a clinically suspicious lesion cannot be excised completely then referral should be made or the lesion should be completely removed.

THE PATHOLOGY REPORT

There are three major risks to consider for a patient with melanomas: local recurrence, lymph node recurrence and distant recurrence.

The information provided by the pathologist in their report is vital in determining these risks and the advice given to patients in regard to prognosis and management.

A combination of the traditional descriptive report and a summary report is preferred. The summary should include the Breslow Thickness (this is the most important), the presence or absence of ulceration, the mitotic rate, the presence of melanomas to the margins and the presence or absence of other features such as lymphovascular invasion, neurotropism, desmoplasia or satellitosis. Most reports comment on evidence of regression. The depth of regression is not relevant to management. Clinical scores are always reported but have been shown to be unreliable.

SENTINEL LYMPH NODE BIOPSY (SLNB)

This remains controversial. There is no doubt that the presence of melanoma in the Sentinel lymph node (SLN) is the greatest determinant of prognosis. There is evidence that lymph node tumour burden and characteristics of the primary lesion, such as the presence of non-SLN involvement, may in future determine that some patients can safely avoid full lymphadenectomy.

ADJUVANT SYSTEMIC TREATMENT

Unlike many types of cancer, an effective adjuvant therapy has been found to reduce the risk of melanoma recurrence does not exist. Chemotherapy has failed. Immunotherapy has failed. On testing in the form of vaccines has failed. The only thing that has been shown to reduce the risk of melanoma recurrence is surveillance. Melanoma is currently a trial randomising patients to observation or full lymphadenectomy.

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