

Laboratory Strategy for Evaluation of Pheochromocytoma

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Pheochromocytoma is a rare but potentially lethal tumor derived from the chromaffin cells of the adrenal medulla and the term is also used to refer collectively to tumors derived from neural crest cells, including paragangliomas and neuroblastomas. Symptoms include episodes of extreme hypertension with cardiac arrhythmias, severe headaches and sweating. The incidence of pheochromocytoma is low (less than 0.2%) in hypertensive patients. These tumors secrete catecholamines (epinephrine, norepinephrine, dopamine). The 3-methoxy metabolites of epinephrine and norepinephrine are metanephrine and normetanephrine, respectively and they are collectively referred to as "metanephrines". Metanephrines are stable and are co-secreted directly with catecholamines by pheochromocytomas and other neural crest tumors.

Several biochemical tests have been used over the years to evaluate patients for pheochromocytoma:

- Plasma free metanephrines, fractionated (PFM)
- Plasma free catecholamines, fractionated (PFC)
- 24-hour urine metanephrines, fractionated (UFM)
- 24-hour urine catecholamines, fractionated (UFC)
- 24-hour urine vanillylmandelic acid (VMA)

At Danbury Hospital, these tests are referred to Mayo Medical Laboratories where they are performed by liquid chromatography-tandem mass spectrometry (LC-MS/MS).

Which tests are most effective for evaluation of pheochromocytoma?

There are considerable international and regional differences in the approach to the biochemical diagnosis of pheochromocytoma and still no consensus as to the "best test". Plasma fractionated metanephrines (PFM) has been advocated by some as the best initial test because of its high sensitivity (96-100%) and negative predictive value. However, its specificity is relatively poor at 85-89%; (77% in patients >60 years of age) which greatly limits its positive predictive

FAST FACTS:

- ✚ Pheochromocytoma is rare (incidence <0.2%)
- ✚ 24-hour urine metanephrines and catecholamines are the best tests for patients with low-moderate index of suspicion.
- ✚ Plasma fractionated metanephrines should also be measured in patients with higher index of suspicion and in children.
- ✚ Plasma fractionated catecholamines and 24-hour urine VMA are no longer useful in evaluating patients for pheochromocytoma.
- ✚ Questions? Contact Dr. Sena at 739-7622

value, particularly when the clinical index of suspicion for a catecholamine-secreting tumor is not high - it has been estimated that 97% of hypertensive patients seen in a tertiary care clinic who have a positive PFM test will not have a pheochromocytoma. A widely referenced Mayo Clinic study found that a combination of 24-hour urine fractionated metanephrines (UFM) and 24-hour urine fractionated catecholamines (UFC) provided the most reliable method for identifying catecholamine-secreting tumors (sensitivity 98%, specificity 98%). A positive test is considered to be a two-fold elevation above the upper reference limit in urine catecholamines or metanephrines.

PFM should also be measured with UFM and UFC when there is a high index of suspicion (family history of pheo, patients with familial endocrine syndromes, history of resected pheochromocytoma with recurrent hypertension, incidentally discovered adrenal mass with imaging characteristics consistent with pheochromocytoma). PFM may also be the preferred test in children because of the inherent difficulty in obtaining a complete 24-hour urine collection.

Plasma fractionated catecholamines (PFC) no longer have a role in evaluating patients for pheochromocytoma due to low sensitivity (84%), as catecholamines may not be continuously secreted and may only be episodically elevated during a “spell”. Also, the specificity of PFC for pheochromocytoma is only 81%. Patient anxiety before venipuncture is a common cause of false elevations and this test requires insertion of an indwelling IV catheter with blood drawn only after the patient has been at rest in the supine position for 30 min. Likewise, 24-hour urine VMA has poor diagnostic sensitivity (64%) and specificity compared to 24-hour urine metanephrines and is no longer considered a useful test.

References

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