

# AMPATH LAB UPDATE

## Urine methylhistamine

Histamine turnover increases due to increased activity (allergic reactions) or proliferation (mastocytosis) of mast cells<sup>1</sup> or basophils<sup>2</sup>. Histamine is released intermittently and has a short half-life, thus measurement of urine 1-methylhistamine (N-Tele-methylhistamine, 1-MHIS), a major metabolite of histamine, has better sensitivity and specificity. Urine 1-MHIS testing is available at Ampath Esoteric Sciences by GC-MS/MS methodology.<sup>3</sup>

### Indications<sup>1</sup>

- Screening for and monitoring of mast cell disorders (mastocytosis, mast cell activation syndrome, systemic allergic reactions).
- Monitoring of therapeutic progress in conditions with low-grade persistent mast cell proliferation and activation.

### Limitations

- Not all patients with mast cell disorders will have increased urinary 1-MHIS.<sup>1</sup>
- Causes other than mast cell disorders for elevated 1-MHIS:  
Non-compliance with histamine-free diet, certain medications, myeloproliferative disorders, carcinoid syndrome, insulinoma, medullary thyroid carcinoma, pheochromocytoma, VIPoma, glucagonoma, scombroidosis, bacterial formation of histamine from histidine in urine.<sup>4</sup>

**Mast cell disorders** present with symptoms of mast cell activation, including flushing, pruritus, urticaria, angioedema, nasal congestion, rhinorrhoea, wheezing, bronchospastic cough, headache, diarrhoea, gastric hyperacidity, abdominal cramping, nausea and vomiting, hypotension and tachycardia.<sup>5</sup>

**Mastocytosis** is a rare group of disorders with neoplastic mast cells in >1 organ systems. Symptoms may include itching, gastrointestinal symptoms, bone pain, headaches, flushing and anaphylaxis.

### WHO classification of mastocytosis 2016<sup>6</sup>

- **Cutaneous mastocytosis:** Urticaria Pigmentosa (UP) is the most common form. Mast cell infiltration causes multiple persistent, small, flat or slightly elevated red-brown skin lesions.<sup>1</sup>
- **Systemic mastocytosis (SM):** Benign or malignant mast cell infiltration of bone marrow, liver, spleen, small intestine or lymph nodes occurs. Benign pediatric SM often resolves over time, while adult SM tends to be progressive. UP may or may not present concomitantly with SM.<sup>1</sup> Diagnosis requires one major and one minor or three minor SM criteria.<sup>6</sup>  
**Major criterion:** Multifocal clusters of 15+ abnormal mast cells in bone marrow or extracutaneous organ(s).  
**Minor criteria:** More than 25% atypical mast cells in bone marrow or spindle-shaped in organs, the presence of KITD816V-point mutation, abnormal mast cell expression of CD25 and/or CD2, elevated serum tryptase level.
- **Mast cell sarcoma** (rare local tumor with poor prognosis)

**Mast cell activation syndrome<sup>7</sup>** describes a clinical presentation, rather than a specific diagnosis and requires three criteria:

- Episodic, objective signs and symptoms involving >2 organ systems
- Laboratory evidence of systemic mast cell-mediator release when symptomatic (e.g. serum tryptase or urine 1-MHIS)
- Response to medications that inhibit the actions of mast cell mediators

<sup>1</sup> <https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/83011>

<sup>2</sup> [http://www.palms.com.au/php/labinfo/info\\_index.php?tab=1](http://www.palms.com.au/php/labinfo/info_index.php?tab=1)

<sup>3</sup> Martens-Lobenhoffer, J. et al., 1999. Determination of 1-methylhistamine and 1-methylimidazoleacetic acid in human urine as a tool for the diagnosis of mastocytosis. *Journal of Chromatography B* 721:135-140

<sup>4</sup> <https://emedicine.medscape.com/article/2093933-overview#showall>

<sup>5</sup> [https://www.uptodate.com/contents/image?imageKey=ALLRG%2F98373&topicKey=ALLRG%2F15715&search=mast%20cell%20activation%20syndrome&rank=1-77&source=see\\_link](https://www.uptodate.com/contents/image?imageKey=ALLRG%2F98373&topicKey=ALLRG%2F15715&search=mast%20cell%20activation%20syndrome&rank=1-77&source=see_link)

<sup>6</sup> Valent, P. et al., 2017. Mastocytosis: 2016 updated WHO classification and novel emerging treatment concepts. *Review. Blood* 129(11):1420-1427

<sup>7</sup> [https://www.uptodate.com/contents/mast-cell-disorders-an-overview?search=mast%20cell%20activation%20syndrome&sectionRank=2&usage\\_type=default&anchor=H2367015693&source=machineLearning&selectedTitle=1-77&display\\_rank=1#H2367015693](https://www.uptodate.com/contents/mast-cell-disorders-an-overview?search=mast%20cell%20activation%20syndrome&sectionRank=2&usage_type=default&anchor=H2367015693&source=machineLearning&selectedTitle=1-77&display_rank=1#H2367015693)

# AMPATH LAB UPDATE

## Urine methylhistamine testing

### Patient preparation

**Diet:** Patient to follow a histamine-free diet for 24 hours prior to and during urine collection.<sup>8</sup>

#### Avoid:

**Fruit:** bananas, canned and fresh pineapples, plums, grapes, kiwifruit, cherries, blueberries, raspberries, strawberries, blackcurrants, citrus, guava, mango, passionfruit, dried fruit

**Jams:** all except apricot

**Vegetables:** tomatoes, mushrooms, avocado, spinach, broccoli, Brussels sprouts, cauliflower, eggplant, broad beans, pickled vegetables (eg. sauerkraut)

**Nuts and seeds:** including peanut butter, tahini, muesli containing nuts or above fruits

**Dairy:** all cheese and cheese spreads, yoghurt (chocolate/nut), flavoured milk (banana, strawberry, chocolate), fruit smoothies

**Fish and seafood:** including canned, dried, salted fish and seafood

**Chocolate, cocoa and Milo**

**Processed meats:** salami, sausages, ham, chicken loaf, etc.

**Condiments:** chutney, malted vinegar, mayonnaise, tartare sauce

**Fermented foods:** yeast extracts (eg. Marmite, Bovril, fish sauce, soy sauce, meat gravy)

**Alcohol:** all wine and beer (all fermented beverages)

#### Allowed:

**Bread and cereal:** plain bread or cereal, wholemeal or white flour products except if containing nuts, seeds, fruit, flavourings or fillings listed above

**Fresh fruit:** apples, pears, apricots, peaches, rockmelon, watermelon

**Vegetables:** all fresh vegetables not listed in foods to avoid

**Coconut and coconut milk**

**Dairy:** fresh milk, fresh cream, vanilla yoghurt, plain ice cream and custard

**Meat and chicken:** freshly prepared,

**Powdered stock:** for gravy, only if freshly prepared

**Sugar:** brown or white

**Spreads:** apricot jam and honey

**Clear vinegar, vanilla and nutmeg**

**Drinks:** milk, milkshakes (vanilla, coffee, plain, caramel), lemonade, tea, coffee

**Medication that may affect 1-MHIS:** Write all current medication on request form.

**NB:** The patient should not stop any medication unless instructed by the treating clinician.

False increase: MAOI antidepressants, test not recommended.

False decrease (Diamine oxidase inhibitors): CHLOROQUINE CLAVULANIC ACID CIMETIDINE VERAPAMIL Acetylcysteine, Aminophylline, Amitriptyline, Colistin, Cyclophosphamide, Diazepam, Dihydralazine, Framycetin, Furosemide, Haloperidol, Isoniazid, Metoclopramide, Neomycin, Orciprenaline, Pancuronium, Pentamidine, Prilocaine, Propafenone, Promethazine, Quinidine, Thiamine/Vitamin B1, Thiopental<sup>9</sup>

**Specimen:** 24-hour urine specimen (MHISU24). Keep urine in the refrigerator during collection.

No preservative needed; Boric acid or HCl preservative is accepted.

24-hour collection is preferred: less variation, less influenced by diet.

Random urine (MHISUR) is accepted.

**Stability:** Room temperature: 24 hours; Refrigerator: 8 days; Frozen: 2 weeks

**Turn-around-time:** 7 days

<sup>8</sup> <https://www.clinicallabs.com.au/patient/collection-information/collection-guide/urine-collection/24hr-urine-for-histaminemethylhistamine/>

<sup>9</sup> Leitner et al., 2014. *Clinical and Translational Allergy* 4(3). Available at: P23 [https://www.histaminintoleranz.ch/en/therapy\\_medicaments.html#dao](https://www.histaminintoleranz.ch/en/therapy_medicaments.html#dao)