

## Overview

### Useful For

Direct measurement of Angiotensin II (Ang II) and Angiotensin (1-7) (Ang 1-7) in plasma Adjunct to plasma renin activity (PRA) and aldosterone measurements for the diagnosis of primary aldosteronism and renal-vascular hypertension. Adjunct, or alternative to, PRA for investigations of potential associations with outcomes of coronavirus infection. Drug studies as to renin-angiotensin system (RAS) manipulations that might be useful in treatment of cardiovascular diseases or corona virus infection. This test is not useful for establishing eligibility for a specific treatment as results must be interpreted in conjunction with the clinical status of the patient.

### Special Instructions

- [Renin-Aldosterone Studies](#)
- [Steroid Pathways](#)

### Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA

### Specimen Required

**Patient Preparation:** Results used for primary aldosteronism may not be interpretable if the patient is being treated with spironolactone (Aldactone). Spironolactone should be discontinued for 4 to 6 weeks before testing. See Cautions for more information.

**Collection Container/Tube:** Chilled, lavender top (EDTA)

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 2 mL

### Collection Instructions:

1. Draw blood in a chilled syringe from a patient in a seated position; place specimen in a chilled, lavender-top (EDTA) tube; and mix.
2. Alternatively, draw blood directly into a chilled, lavender-top (EDTA) tube.
3. Immediately place EDTA tube into an ice-water bath until thoroughly cooled.
4. Refrigerate specimen during centrifugation and immediately transfer plasma to plastic vial. If a refrigerated centrifuge is unavailable, chill the centrifuge carriers. Centrifuge specimen, then promptly transfer plasma.
5. Immediately freeze plasma.

### Specimen Minimum Volume

1.25 mL

### Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen	28 days	

## Clinical and Interpretive

### Clinical Information

Direct Angiotensin II (Ang II) if preferable since the final pathway of renin activation is the generation of Ang II by the Angiotensin converting enzyme 2 (ACE2) receptor.

The angiotensins (Ang): Ang I (Ang 1-10), Ang II (Ang 1-8), Ang III (Ang 2-8), Ang IV (Ang 3-8), Ang 1-9, Ang 1-7, Ang 1-5, and Ang 1-4 are signaling peptides that are activated through feedback regulated peptidase cascades. Currently, Ang II, Ang III, Ang IV, and Ang 1-7 are considered biologically active with both overlapping and differential actions.

Angiotensins are involved in the regulation of almost 100 different biological processes. However, their most prominent effects are regulation of vascular tone and aldosterone secretion.

The first step in the angiotensin cascade is mediated by renin, which is produced by the renal juxtaglomerular apparatus in response to increased renal sympathetic activity, reduced renal blood pressure, or decreased sodium and chloride concentrations. Renin cleaves the secreted portion (amino acids 34-485) of angiotensin precursor protein angiotensinogen near its N-terminus. The resultant decapeptide, Ang I, is devoid of biological activity but serves as the reservoir/precursor for the bioactive downstream peptides that are generated by angiotensin converting enzyme 1 (ACE).

Traditionally, serum or plasma aldosterone and plasma renin activity (PRA) measurements (amount of Ang I generated per hour at 37 degrees C) have been used to assess the renin-angiotensin system (RAS) in order to assist in the diagnosis of primary aldosteronism (low PRA, high aldosterone) and renal vascular disease (high PRA, high aldosterone).

More recently, there has been increasing interest in direct measurement of Ang II, the most bioactive compound that mediates most of the vasoconstriction via Ang II receptors type 1 and 2, and of Ang 1-7, which has opposing effects through competitive binding to the Ang II receptor and via signaling through the separate MAS1 proto-oncogen receptor (MAS1). Ang 1-7 is one of the Ang II degradation products that are generated by the soluble and membrane-bound variants of angiotensin converting enzyme (ACE2). Direct measurement of Ang II, or of the combination Ang II and Ang 1-7, potentially provides a better estimation of the biological effects of RAS activation than PRA.

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With possible discontinuation of angiotensin-receptor blockers and ACE inhibitors in patients, therapeutic monitoring and further assessments of RAS or renin-angiotensin-aldosterone system (RAAS) may be necessary.

In addition, coronaviruses, including highly pathogenic variants such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and SARS-coronavirus 2 (SARS-CoV-2) effect entry into cells by binding to membrane-bound ACE2, mimicking Ang II binding through their spike proteins. This is followed by ligand dependent endocytosis of the virus. The balance of Ang II and Ang 1-7, and of their respective receptors, in the vicinity of virus-exposed cells, regulates the endocytotic process in an incompletely understood fashion. This has generated intense interest in examining whether ACE inhibitors, Ang II receptor blockers, or other novel drugs might be able to reduce viral entry. In addition, Ang II or Ang 1-7 concentrations and the degree of respective ACE and ACE2 activity might predict severity of coronavirus infections.

### Reference Values

Angiotensin II: <5-40 pg/mL

Angiotensin (1-7): <10-55 pg/mL

### Interpretation

High angiotensin II (Ang II) concentrations in the absence of angiotensin receptor blockers (ARB) therapy are suggestive of angiotensin-driven hypertension.

Low Ang II concentrations in conjunction with low plasma renin activity (PRA) and high serum/plasma aldosterone concentration indicate possible primary aldosteronism. Conversely, if aldosterone is low, renal vascular disease should be suspected.

Simultaneous angiotensin (1-7) (Ang 1-7) measurement might allow further assessment of the biological consequences of Ang II signaling, with high Ang 1-7 concentrations suggesting that some of the pressor effects are ameliorated via MAS1 protooncogene signaling by Ang 1-7.

For experimental and clinical trial studies for cardiovascular disease and prediction of likely coronavirus infection severity, there are, at the moment, no definitive guidelines and results should be interpreted in the context of each study.

Test results are to aid the interpretation of clinical status and optimal paths for further investigation, if any. Test results should always be interpreted in conjunction with all other clinical findings as they cannot be interpreted as absolute evidence for the presence or absence of disease.

**Note:** Advice on stimulation or suppression tests is available from Mayo Clinic's Division of Endocrinology and may be obtained by calling 800-533-1710. See [Renin-Aldosterone Studies](#) and [Steroid Pathways](#) in Special Instructions.

### Cautions

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARB) have the potential to impact angiotensin II levels in plasma. Patient should be on a normal sodium diet. It may be beneficial to have patient seated in a recumbent posture if possible for at least 30 minutes prior to collecting specimen. Steroids, estrogens, oral contraceptives, ACT medications, and diuretics will all affect angiotensin II levels as will posture along with sodium, potassium, and multivitamins. Results used for primary aldosteronism may not be interpretable if the patient is being treated with spironolactone (Aldactone). Spironolactone should be discontinued for 4 to 6 weeks before testing.

### Clinical Reference

1. Arendse LB, Jan Danser AH, Poglitsch M, et al: Novel therapeutic approaches targeting the renin-angiotensin system and associated peptides in hypertension and heart failure. *Pharmacol Rev.* 2019 Oct;71(4):539-570

2. Bader M, Alenina N, Young D, Santos RAD, Touyz RM: The Meaning of Mas. Hypertension. 2018 Nov;72(5):1072-1075. doi: 10.1161/HYPERTENSIONAHA.118.10918
3. Deshotels MR, Xia H, Sriramula S, Lazartigues E, Filipeanu C: Angiotensin II mediates angiotensin converting enzyme type 2 internalization and degradation through an angiotensin II type I receptor-dependent mechanism. Hypertension. 2014 Sep;64(6):1368-1375
4. Guo Z, Poglitsch M, McWhinney C, et al: Measurement of equilibrium angiotensin II in the diagnosis of primary aldosteronism. Clin Chem. 66(3):483-492
5. Hoffmann M, Kleine-Weber H, Schroeder S, et al: SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020 Apr 16;181(2):271-280. doi:10.1016/j.cell.2020.02.052
6. Santos RAS, Sampaio WO, Alzamora AC, et al: The ACE2/Angiotensin-(1-7)/MAS Axis of the Renin-Angiotensin System: Focus on Angiotensin-(1-7). Physiol Rev. 2018 Jan 1;98(1):505-553. doi: 10.1152/physrev.00023.2016
7. South AM, Tomlinson L, Edmonston D, Hiremath S, Sparks M: Controversies of renin-angiotensin system inhibition during the COVID-19 pandemic. Nat Rev Nephrol. 2020;16(6):305-307. doi: 10.1038/s41581-020-0279-4

## Performance

### Method Description

Angiotensin II and Angiotensin (1-7) are extracted from EDTA plasma with internal standard and then analyzed by liquid chromatography-tandem mass spectrometry.(LC-MS/MS).(Unpublished Mayo Method)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Varies

### Analytic Time

2 days

### Maximum Laboratory Time

5 days

### Specimen Retention Time

14 days

### Performing Laboratory Location

Rochester

## Fees and Codes

### Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

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**Test Classification**

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

**CPT Code Information**

82163

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
ANGII	Angiotensin II and Ang (1-7), P	95515-3

Result ID	Test Result Name	Result LOINC Value
609051	Angiotensin II	1860-6
609417	Angiotensin (1-7)	95516-1