The Warde Report

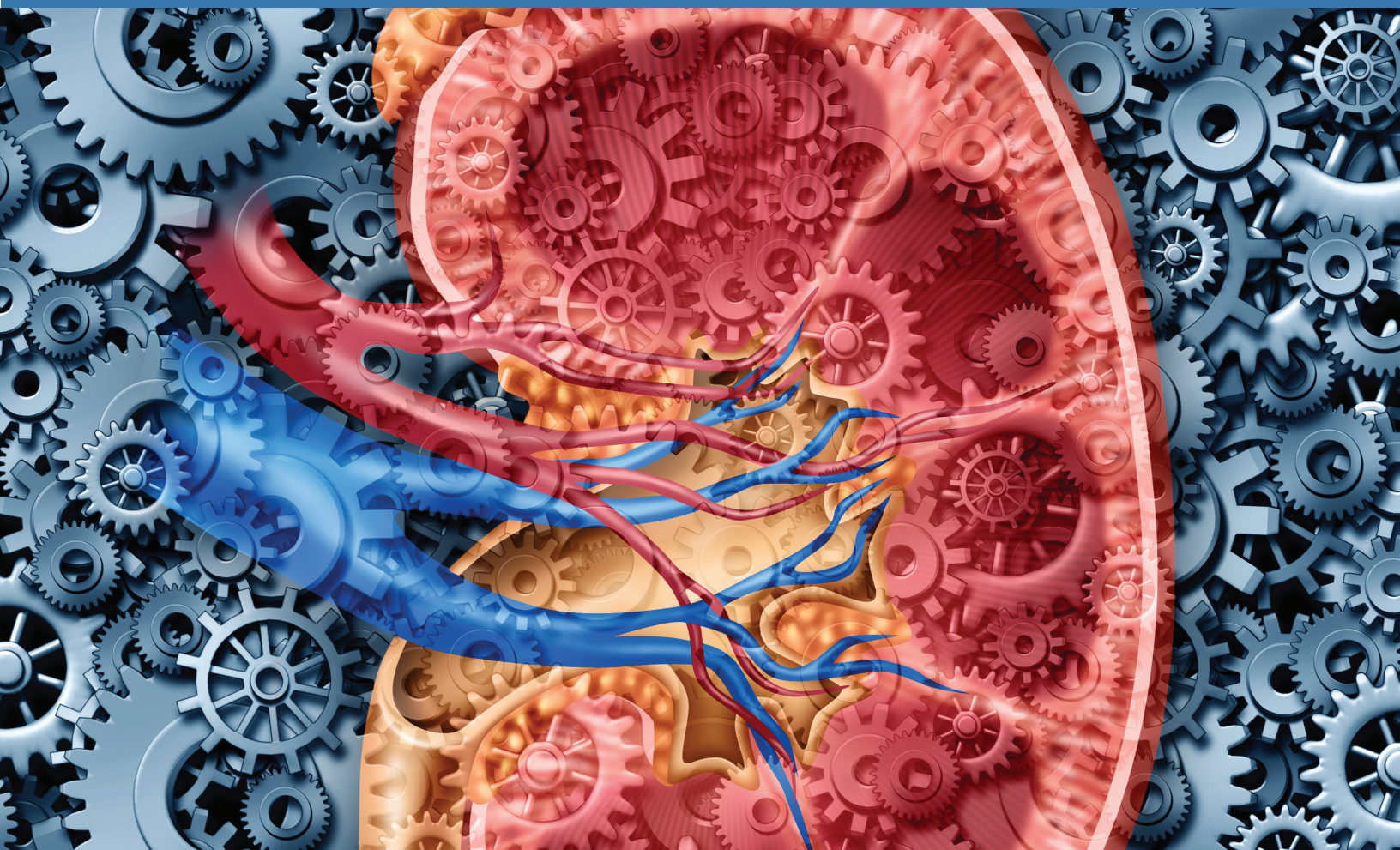
A Publication of Warde Medical Laboratory
Issue Number 27, Volume 1, 2017
Modified May 2020

Test Update: **Renin and Aldosterone/Renin Ratio**

Also in This Issue

Measurement of Lead Levels in Blood

"Quality in Laboratory Diagnosis"



Test Update:
Renin and Aldosterone/Renin Ratio

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The determination of renin is useful for the investigation of secondary aldosteronism (e.g. renovascular disease, salt depletion, potassium loading, cardiac failure with ascites) or for the investigation of primary aldosteronism (adrenal adenoma/carcinoma and adrenal cortical hyperplasia).

Renin can be measured as the plasma renin activity (PRA) or the direct renin concentration (DRC). Both are approved for clinical use in a recent Endocrine Society Practice Guideline, either by themselves or combined with aldosterone to obtain an aldosterone to renin ratio [1].

However, the sole manufacturer of the FDA approved assay kits for plasma renin activity discontinued their manufacture in December 2016. As a result, Warde Medical Laboratory validated an FDA approved kit for direct renin concentration and has converted to the methodology effective January 24, 2017.

The new assay measures the actual concentration of renin. The units are pg/mL. The old assay (Plasma Renin Activity) measured the activity of renin by measuring the production of Angiotensin 1 under controlled conditions. As an enzyme assay, it was dependent upon pH, incubation time, substrate concentration, and the presence of inhibitors or catalysts (including drugs). The units were ng/mL/hr.

PRA and DRC measures of renin are both approved either by themselves or in combination with aldosterone to obtain an aldosterone to renin ratio.

There is no precise conversion factor between the two different methods. That being said, and although it varies from patient to patient, 1 ng/mL/hr of plasma renin activity approximately equals 7.6 pg/mL of direct renin concentration (range 5.5 to 9.7). So one will see higher "renin" values with the new assay.

A number of clinical studies have validated the use of the direct renin assay in screening for primary aldosteronism [2,3,4,5]. In one study, at an aldosterone/ direct renin ratio of greater than 3.7 (37.0 in conventional units), the sensitivity was 90% and the specificity was 100% [2].

The advantages of this new method are:	
1	Improved low end sensitivity.
2	Improved between lab standardization as this method is calibrated against the WHO IS 68/356 standard.
3	Less sample required.
4	Less interference from hemolysis. With the plasma renin activity assay, any hemolysis was unacceptable, but mild to moderate hemolysis is acceptable with the new direct renin assay.
5	When used with aldosterone to screen for primary aldosteronism, fewer false positives. [2]

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Measurement of Lead Levels in Blood

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A renewed public interest in lead toxicity was spurred by the water crisis in Flint, Michigan in 2014.[1] In an effort to save money, a state-appointed emergency manager established plans to change the Flint water supply from water purchased from the Detroit Water and Sewerage Department to a new pipeline under construction in Lake Huron.

Today it is broadly recognized that lead serves no beneficial function to human life, and that there is no such thing as a safe level of lead exposure.

Pending completion of that pipeline, the Flint water supply was temporarily switched to the Flint River as its principal source. The new source yielded water that was more corrosive than the existing source, resulting in the leaching of lead from the antiquated system of pipes that constituted the Flint water distribution system. As a result, the number of children in Flint with elevated blood levels essentially doubled, from 2.4% prior to the switch to 4.9% after the switch.[1]

Historical Perspective

Recognition of lead poisoning dates back thousands of years.[2] Anemia, encephalopathy, "lead palsy," and "lead colic" are some of the oldest known manifestations of lead poisoning. However, the recognition of lower level lead exposure as an ongoing environmental and public health threat is a relatively recent phenomenon.

For centuries, lead control efforts were aimed at preventing ingestion or exposure to clinically toxic lead levels, with little awareness of the risk of lower level or chronic environmental lead exposure. Today it is broadly recognized that lead serves no beneficial function to human life, and that there is no such thing as a safe level of lead exposure.[2,3]

Attempts to monitor and control lead poisoning in industrial workers in the early 20th century paved the way for modern occupational health initiatives, developed through such works as Legge and Goadby's Lead Absorption in 1912,[2,4] and by the pioneering work of Alice Hamilton—cited by some as the inventor of "industrial medicine."[2,5] Still, however, the focus was mainly on the detection and management of frank toxicity, rather than prevention.

Unfortunately, awareness of the deleterious effects of even low-level lead exposure didn't develop until the latter part of the 20th century. The development of this awareness was hampered by the activism of commercial interests (particularly in the petroleum industry), and by the nearly ubiquitous contamination of laboratory equipment and operators by environmental lead (likely due to the use of tetraethyl lead as a gasoline additive dating to the 1920s).[2]

This widespread contamination resulted in the interpretation of baseline lead levels observed in individuals and in the environment as natural rather than man-made.

Dr. Clair Patterson, a geologist whose interest in lead began with his research on the calculation of the age of the Earth, published compelling evidence that lead levels deemed "natural" by others in the field (including Robert Kehoe, a leading skeptic of Patterson's work who did not believe in the concept of subclinical lead poisoning) were actually the result of man-made environmental pollution, and orders of magnitude higher than truly natural environmental levels.[6]

Surprisingly, the two greatest contributors to lead toxicity in modern society—the use of lead-based paint and the use of tetraethyl lead as a gasoline additive—were only banned in the United States in 1978 and 1996, respectively (although a gradual phase-out of tetraethyl lead had begun some two decades earlier). Today, exposure to lead paint in houses built before 1978 remains a principal source of childhood lead poisoning.

CDC Guidelines

Prior to 2012, the Centers for Disease Control and Prevention (CDC) had established a whole blood lead concentration of 10 ug/dL as a "level of concern" for the screening of children for lead toxicity. However, in 2012 the CDC's Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) recommended that the term "level of concern" be eliminated from all guidance documents, since cognitive deficits are well documented in children whose peak blood levels never exceeded 10 ug/dL, and since there is a growing consensus that no level of lead exposure is considered safe.[3]

The ACCLPP recommended instead the establishment of a childhood blood lead reference value of 5 ug/dL to "identify children and environments associated with lead exposure hazards" based on the 97.5th percentile of childhood lead levels according to the CDC's National Health and Nutrition Examination Survey (NHANES). The Committee further recommended that this reference level be reviewed periodically based on population data.

Screening for Elevated Lead Levels

Measurement of whole blood lead is the recommended method for screening for lead exposure and toxicity.[3] While the measurement of zinc protoporphyrin (ZPP) level may be useful in assessing the chronicity of lead toxicity in the setting of known occupational or industrial exposure, ZPP lacks both sensitivity and specificity in assessing for environmental exposure or more acute lead toxicity[7] and is not recommended for populational screening.

The World Health Organization (WHO) and the Clinical and Laboratory Standards Institute (CLSI) recognize three main methods for the determination of blood lead levels: atomic absorption spectrometry (AAS), anodal stripping voltammetry (ASV), and inductively coupled plasma mass spectrometry (ICP-MS).[8,9]

While ASV has gained popularity due to its relative ease of use and adaptability to portable or point-of-care platforms, it is relatively insensitive, with detection limits (particularly in point-of-care applications) that may not satisfy the current CDC recommendations for whole blood lead level detection.

Warde Medical Laboratory currently uses a graphite furnace AAS method that is highly sensitive and provides rapid results for the accurate determination of blood lead levels.

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