

Nicotine & Metabolites

Clinical Background

Use of tobacco products, particularly smoking, is a leading but preventable cause of disease, disability and death.

Epidemiology

- Prevalence – 15-20% of adults are nicotine dependent
- Sex – M>F

Pathophysiology

- Nicotine is found in a variety of plants
- Principle source of exposure – tobacco products or nicotine replacement therapy
- Extensively metabolized by the liver
- Increases heart rate, blood pressure, mobilization of blood sugars and catecholamines
- Absorbed through oral cavity, skin, urinary tract and gastrointestinal tract

Clinical Presentation

- Cancers – lung, larynx, oral and nasal cavity, paranasal sinuses, esophagus, pancreas, liver, stomach, cervix, leukemia
- Cardiac and neurologic disease – a leading cause of coronary disease, stroke
- Pulmonary disease – chronic obstructive pulmonary disease (includes chronic bronchitis and emphysema), asthma, respiratory infections, overall decrease in pulmonary function
- Pregnancy – difficulty in conceiving, intrauterine growth retardation, low birth weight
- Second-hand smoke (a confirmed human carcinogen) – implicated in pulmonary disease, lung cancer and coronary artery disease in non-smokers

Diagnosis

- Indications for testing – documented tobacco use
- Laboratory testing
 - Urine testing recommended over serum/plasma testing to detect chronic use
 - Nicotine and related compounds are detected over a longer period of time in urine and can differentiate among the following:
 - Active user
 - Abstinent user of >2 weeks
 - Passive exposure
 - Unexposed non-tobacco user
 - Anabasine in urine indicates that donor is actively using a tobacco product; anabasine is not expected in nicotine replacement products
 - Serum plasma testing is required when a valid urine specimen cannot be obtained (anuretic or dialysis patient) or to detect recent use (within past 2 weeks)

Pharmacogenetics and Therapeutic Drug Monitoring

- Nicotine is extensively metabolized in the liver
 - 70-80% converted to cotinine
 - Mediated by cytochrome P450 system (mainly CYP2A6 and CYP2B6)
 - Also metabolized to nor nicotine
 - Cotinine further metabolized

- Trans-3'-hydroxycotinine – main metabolite detected in urine
- Anabasine – minor tobacco alkaloid
 - Used to check compliance with nicotine replacement therapy
- Monitoring of patient for tobacco cessation
 - Measurements in urine for nicotine, cotinine, hydroxycotinine, nornicotine and anabasine
 - Plasma measurement cannot differentiate nicotine patch from tobacco reinstatement

Monitoring

- Helpful in the following situations
 - Compliance with requirements in smoking cessation programs
 - Candidates for orthopedic surgery (particularly spinal fusion), pulmonary therapy and organ transplant programs
 - Identification of tobacco-using patients
- Experimental nicotine therapy in cognitive degeneration disorders, eg, Alzheimer disease, Parkinson disease and attention deficit/hyperactivity disorder (ADHD)

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
Nicotine & Metabolites, Urine 0092356 Method: Liquid Chromatography-Tandem Mass Spectrometry	Detect nicotine, cotinine, trans-3'-hydroxycotinine, nornicotine and anabasine in urine Identify presence of anabasine which identifies use of tobacco products Distinguish between categories of tobacco exposure and/or use – unexposed non-tobacco users, passively exposed, abstinent users (>2 weeks) and active users	Absence of expected drug(s) and/or drug metabolite(s) may indicate non-compliance, inappropriate timing of specimen collection relative to drug administration, poor drug absorption, or limitations of testing Interpretive questions should be directed to laboratory	

<p>Nicotine & Metabolites, Serum or Plasma 0092361 Method: Liquid Chromatography-Tandem Mass Spectrometry</p>	<p>Detect and monitor nicotine, cotinine, and trans-3'-hydroxycotinine in serum or plasma Order for patients when a valid urine specimen cannot be obtained (eg, anuretic or dialysis patient)</p>	<p>Absence of expected drug(s) and/or drug metabolite(s) may indicate non-compliance, inappropriate timing of specimen collection relative to drug administration, poor drug absorption, or limitations of testing Interpretive questions should be directed to laboratory Does not detect anabasine</p>	
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Guidelines

Practice guideline for the treatment of patients with substance use disorders. American Psychiatric Association - Medical Specialty Society. 1995 (Revised 2006 August).

Treating tobacco use and dependence: 2008 update. Public Health Service (U.S.) - Federal Government Agency [U.S.]. 1996 (Revised 2008 May).

General References

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Hughes JR, Helzer JE, Lindberg SA. Prevalence of DSM/ICD-defined nicotine dependence. *Drug Alcohol Depend.* 2006; 85 (2) :91-102.

Moyer TP, Charlson JR, Enger RJ, Dale LC, Ebbert JO, Schroeder DR, Hurt RD. Simultaneous analysis of nicotine, nicotine metabolites, and tobacco alkaloids in serum or urine by tandem mass spectrometry, with clinically relevant metabolic profiles. *Clin Chem.* 2002; 48 (9) :1460-1471.

Tobacco use--United States, 1900-1999. *MMWR Morb Mortal Wkly Rep.* 1999; 48 (43) :986-993.

Tutka P, Mosiewicz J, Wielosz M. Pharmacokinetics and metabolism of nicotine. *Pharmacol Rep.* 2005; 57 (2) :143-153.

Yildiz D. Nicotine, its metabolism and an overview of its biological effects. *Toxicol.* 2004; 43 (6) :619-632.

Reviewed by

McMillin, Gwen, PhD. Medical Director of Clinical Drug Abuse Testing, Clinical Toxicology and Trace Elements, Co-Medical Director for Pharmacogenomics at ARUP Laboratories; Assistant Professor of Pathology (Clinical), University of Utah

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