Name of Policy:
End-Tidal Carbon Monoxide Measurement (ETCOc)

Policy #: 196
Category: Laboratory
Latest Review Date: August 2010
Policy Grade: Active Policy but no longer scheduled for regular literature reviews and updates.

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**
The measurement of ETCOc corrected for background carbon monoxide (CO) in the breath represents a new technology that is said to detect the rate of hemolysis and/or assist in the tracking of hemolytic conditions. The technology is said to also measure end-tidal carbon dioxide (ETCO2) and respiratory rate simultaneously. The test is non-invasive, does not require the cooperation of the patient, and the results are available immediately.

The catabolism of hemoglobin (Hgb) results in the equimolar formation of CO and Bilirubin. ETCOc is an indicator of the rate of hemolysis and bilirubin production. Elevation of breath CO may be indicative of pathological process in the newborn.

Administration of the test involves placement of a catheter into a patient’s nostril, secured to the lip with tape; insertion of filter cartridge to analyzer port; and sampling of patient’s breath with background air check for base levels. An elevated ETCOc is said to indicate that the infant is at high risk for development of hyperbilirubinemia. The cause of the hemolysis should be identified, appropriate treatment should be initiated, and the patient should be monitored closely.

Jaundice is probably the most common medical issue in newborns, affecting 60% to 70% of children within the first week of life. It is one of the most common diagnoses for readmission of newborns. Although all babies have levels higher than adults do, neonatal hyperbilirubinemia is considered when total serum bilirubin (TSB) level is >5 mg/dL. Bilirubin is formed from the breakdown of hemoglobin and hemoproteins. There is equimolar production of carbon monoxide (which is exhaled) and bilirubin (which is excreted in the GI tract). Bilirubin excess occurs due to overproduction, decreased conjugation, or impaired excretion/increased reabsorption.

The examining clinician who notices jaundice or scleral icterus often first detects hyperbilirubinemia. Jaundice typically begins in the face and spreads to the chest and the extremities. Visual examination (largely dependent on experience, skin tone, and lighting) may not be reliable. Jaundice within the first 24 hours is pathologic and requires immediate evaluation and therapy. More typically, jaundice appears on day of life 2 to 4 and is often idiopathic.

The diagnosis of hyperbilirubinemia is based on TSB. Transcutaneous bilimeters offer advantages in ease, cost, and comfort to the patient. The newer models may not be as dependent on skin pigmentation, which is the biggest obstacle in using these devices. End tidal carbon monoxide levels is said to help assess for increased production of bilirubin, but this method has not been shown to be clinically superior to hour-specific bilirubin levels in the prediction of hyperbilirubinemia.
Policy:
End-Tidal Carbon Monoxide measurement as an index of bilirubin production and/or hemolysis does not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered investigational.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members’ contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:
While measurement of end-tidal carbon monoxide levels, an index of bilirubin production can provide information about the presence or absence of hemolysis, additional research is needed to quantify the risks, benefits, and costs of these measurements. Until such information is available, the American Association of Pediatrics practice guidelines represent a good approach for most infants.

Three studies described the comparison of ETCOc as a single measurement or in combination with total serum bilirubin (TSB) measurements, to predict the development of hyperbilirubinemia during the first 7 days of life. Stevenson reported results from a study of 1370 neonates in a yearlong cohort study. Measurements of both ETCOc and TSB were performed at 30 +/- hours of live; TSB also was measured at 96 +/- 12 hours. A total of 120 (8.8%) of the enrolled infants became hyperbilirubinemic. The ETCOc at 30 +/- 6 hours for the total population was 1.48 +/- parts per million (ppm), whereas those of nonhyperbilirubinemic and hyperbilirubinemic infants were 1.45 +/- 0.47 ppm and 1.81 +/- 0.59 ppm, respectively. Seventy-six percent (92 of 120) of hyperbilirubinemic infants had ETCOc greater than the population mean. Conclusions were that the addition of an ETCOc measurement provides insight into the processes that contribute to the condition but does not materially improve the predictive ability of an hours of age-specific TSB in this study population.

Javier’s study evaluated the clinical usefulness of ETCOc as a single measurement or in combination with total serum bilirubin (TSB) measurements, to predict the development of hyperbilirubinemia during the first 7 days of life. Stevenson reported results from a study of 1370 neonates in a yearlong cohort study. Measurements of both ETCOc and TSB were performed at 30 +/- hours of live; TSB also was measured at 96 +/- 12 hours. A total of 120 (8.8%) of the enrolled infants became hyperbilirubinemic. The ETCOc at 30 +/- 6 hours for the total population was 1.48 +/- parts per million (ppm), whereas those of nonhyperbilirubinemic and hyperbilirubinemic infants were 1.45 +/- 0.47 ppm and 1.81 +/- 0.59 ppm, respectively. Seventy-six percent (92 of 120) of hyperbilirubinemic infants had ETCOc greater than the population mean. Conclusions were that the addition of an ETCOc measurement provides insight into the processes that contribute to the condition but does not materially improve the predictive ability of an hours of age-specific TSB in this study population.

Okuyama did a study to evaluate the value of an end-tidal carbon monoxide corrected for inhaled carbon monoxide concentration at the early neonatal period for use in predicting subsequent hyperbilirubinemia in non-hemolytic full-term infants. Fifty-one infants were enrolled in the
study where seven of the 51 infants developed hyperbilirubinemia. It was concluded that increased ETCO level in the early neonatal period is associated with subsequent hyperbilirubinemia, even in infants without hemolytic disease.

August 2008 Update
Two studies have been published on the use of end-tidal carbon monoxide levels in prematurely born infants predicting bronchopulmonary dysplasia (BPD) or chronic lung disease. May et al, (2007) published a report on end-tidal carbon monoxide levels in premature infants developing bronchopulmonary dysplasia. Inflammatory mediators can induce hemoxygenase-1 with a consequent increase in carbon monoxide (CO) production. ETCO levels would be elevated in infants developing BPD. Serial measurements of ETCO were attempted on d 3, 5, 7, 14, 21, and 28 in 50 prematurely born infants. Fourteen of the infants developed BPD and had higher ETCO levels compared with the rest of the cohort. The authors determined that measurement of ETCO levels in prematurely born infants may be useful in the prediction of development of BPD. Krediet and colleagues (2006) studied the relationship between ETCO and respiratory distress syndrome (RDS) in preterm infants, as well as the value of early ETOC measurements to predict chronic lung disease. Seventy-eight infants (48 had moderate to severe RDS) were included in the study. ETCO was significantly higher in RDS compared to no RDS during the first week. Negative predictive value of early (within the first 12 hours of life) ETCO measurement for development of chronic lung disease was 100%. The authors concluded that during severe RDS, inflammation may contribute to increased lipid peroxidation leading to increased local CO production in the lung, indicated by increased ETCO. Early ETCO determination may be helpful to exclude occurrence of chronic lung disease.

August 2010 Update
In October 2009, the United States Preventive Services Task Force (USPSTF) published a statement on the screening of infants for hyperbilirubinemia to prevent chronic bilirubin encephalopathy. The USPSTF “concluded that the evidence is insufficient to recommend screening infants for hyperbilirubinemia to prevent chronic bilirubin encephalopathy”. It was also determined that the benefits and harms of screening is lacking.

Therefore the policy statement remains unchanged.

Key Words:
End-tidal carbon monoxide levels, ETCOc, hyperbilirubinemia, serum bilirubin, bilirubin, hemolysis, jaundice, transcutaneous bilimeters

Approved by Governing Bodies:
Not applicable

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational. Will be reviewed for medical necessity
Pre-certification/Pre-determination requirements: Not applicable

**Current Coding:**
CPT codes:
- 84999 Unlisted chemistry procedure

**Previous Coding:**
- 0043T Carbon monoxide, expired gas analysis (e.g., ETCOc/hemolysis breath test) *(Code deleted effective January 1, 2009)*

**References:**
3. Herschel, M. Evaluation of the direct antiglobin (coombs’) test for identifying newborns at risk for hemolysis as determined by end-tidal carbon monoxide concentration (ETCOc); and comparison of the coombs’ test with ETCOc for detecting significant jaundice, J Perinatol 2002;22(5):341-7.
Policy History:
Medical Policy Group, August 2004 (4)
Medical Policy Administration Committee, September 2004
Available for comment September 7-October 21, 2004
Medical Policy Group, August 2006 (1)
Medical Policy Group, August 2008 (1)
Medical Policy Group, August 2010 (1) Key points updated
Medical Policy Group, September 2012 (3): Active Policy but no longer scheduled for regular literature reviews and updates.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.