

## Clinical pathology of coma and alteration of consciousness

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*Coma is a common condition in medicine. In this article, the author reviews and discusses important aspects in clinical pathology of coma and alteration of consciousness. Some special concerns and aspects in specimen collections and other laboratory process are also discussed.*

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Acutely ill patients often present with an altered level of consciousness.<sup>(1)</sup> However, there are a number of reasons that may cause the alteration of consciousness and caregivers who are not aware of any defined cerebral activity of the patient need to be aware of the situations that can alter the patient's level of consciousness so that proper strategies of care can be implemented.<sup>(1)</sup> Physiologically, consciousness is a state of awareness of the self and the environment. Consciousness is divided into two components: (1) arousal or wakefulness which is controlled by upper brainstem and hypothalamus/thalamus; (2) content or mental capabilities which is controlled by the cerebral hemispheres. Coma is a state of impaired consciousness in which the patient is unaware of and does not respond to external stimuli. Alterations of consciousness indicate significant brain dysfunction, either from structural lesions, or diffusely active metabolic causes.

The role of clinical pathology is usually related to the metabolic causes of coma. Once a structural cause of coma has been ruled out, then metabolic causes of coma must be investigated. This is the largest group of causes of coma and is investigated by laboratory tests. Metabolic causes of coma include drugs coma, metabolic coma and coma due to major organ failures. The details of laboratory investigation in each condition will be further discussed.

### **Laboratory cycle involving patients with coma and alteration of consciousness**

#### **A. Pre-analytical phase**

Specimen collection in patients with coma and alteration of consciousness is sometimes considerably difficult. Its difficulty is due to the problem of the illness

of the patient as well as the patient's rights. It should be noted that prompt diagnosis of coma depends on collection of critical and archival laboratory specimens before the administration of nonspecific therapy.<sup>(2)</sup> Sometimes, blood collection seems to be difficult due to the sunken of the vascular. Then special venipuncture techniques must be applied. Regarding ethical considerations for getting specimen from comatose patients, retrieving of the specimens must abide by the patients' informed consents. However, the physicians may have their privilege in case of first aids and emergency situations.

#### **B. Analytical phase**

Simple principles of quality management in analytical phase must be used. There are some specific concerns on bed-side test or point-of-care testing. Some point-of-care devices such as glucometer are used in the diagnosis of metabolic coma.

#### **C. post-analytical phase**

Prompt delivery of laboratory results from the laboratory to the physician – in charge is necessary for the management of comatose patients.

### **Laboratory investigation in some important metabolic causes of coma**

#### **1. Drugs**

This is a very common cause of coma. Common drugs that cause coma include alcohol, opiates, and hypnotics. Clinicians in the emergency department are often confronted with comatose patients caused by poisoning.<sup>(3)</sup> An early systematic general approach involving consultation with a

neurologist is of paramount importance.<sup>(3)</sup> A high index of suspicion, a systematic first assessment already in the pre-hospital phase and early stabilization of the vital functions are first essential steps.<sup>(3)</sup> Specific antidotes like hypertonic glucose and thiamine are parts of a “coma cocktail”.<sup>(3)</sup>

The opiate antagonist, naloxone, should be used only when it is clinically indicated and only under titration. Flumazenil should only be used with caution and reserved for restricted cases.<sup>(3)</sup>

For laboratory diagnosis of each condition, specimen collection is the important concern in clinical pathology since there might be some legal problems in these cases. Forensic specimen collection technique must follow. The examiners must be aware of the nuances of forensic evaluation in the context of the conditions of examination, ethics and responsibilities that they have been charged with as an independent evaluator and fact seeker in the context of litigation-oriented dispute resolution.<sup>(4)</sup> To determine alcohol and hypnotics levels, blood specimens are needed. A special caution in blood collection for alcohol level test should be made, i.e., the usage of alcohol for cleansing the venipuncture site must be avoided. A standard operating procedure is necessary to ensure maximum reliability.<sup>(5)</sup> The use of a conversion factor to obtain a calculated “presumed blood level” can be dangerous and should be avoided.<sup>(5)</sup> There are certain time limits for storage of the blood-alcohol specimens. Therefore, each laboratory must establish its own limits for reliable storage, given the conditions in that laboratory.<sup>(5)</sup> In addition, unexpected and confusing results can lead to an erroneous interpretation, especially when history,

circumstances, type of injury, and survival time are not carefully taken.<sup>(5)</sup> As for opiates, urine sample is required for both qualitative and quantitative diagnosis. Communications between the requesting clinician and the laboratory are essential. An advisory service should be provided by the laboratory and clinicians should be encouraged to discuss requests and results with laboratory staff.<sup>(6)</sup> However, it should be remembered that these profiles take a considerable period of time before the results come out. Therefore, the main goal is still the treatment of the patient based on clinical diagnosis.

## 2. Metabolic disturbances

Common metabolic disturbances leading to coma include hyperglycemia or hypoglycemia, hypoxia, severe electrolyte disturbances (Na, K, Ca, and Mg). Therefore, a standard laboratory measurement for patients with coma usually included blood glucose level, blood electrolyte and arterial blood gas. However, some point-of-care testing can be applied such as glucometer for monitoring of finger capillary blood glucose level, which is well correlated with venous blood glucose, and pulse oxymeter to determine the estimated oxygen saturation. In addition to general common metabolic disturbances, some rare disturbance due to specific endocrine disorders such as Addisonian crises and thyroid crises should be in mind if there are additional supportive evidences of these endocrine disorders, and the magnitude of the metabolic disorder, since in these metabolic disturbances, the severity of consciousness impairment is related to both the rate of onset and the magnitude of the metabolic disorder.<sup>(7)</sup>

### 3. Major organ failure

Major organ failures that can manifest as coma include liver failure (hepatic coma), renal failure (uremia + electrolyte disturbance), and chronic lung diseases (hypoxia + hypercarbia). However, most of these major organ failures usually present with a chronic history of underlying illness that can help the diagnosis. Laboratory investigations can confirm definite diagnosis for each suspected condition of corresponding organ failure.

#### Use of the laboratory investigation for comatose patients

Similar to other emergency conditions, laboratory investigation is an essential tool in bring

definite diagnosis. However, the physician should perform first aids and treatment of the patient before making the diagnosis. The diagnosis should start from the classification of the types of coma as structural causes or metabolic causes. If the case is classified into the group of metabolic cause, further laboratory investigation process should be done beginning with routine tests which are useful for diagnosis of metabolic causes of coma due to metabolic disturbances or major organ failure then proceed to special tests which are useful for diagnosis of metabolic causes of coma due to drugs. As a laboratory guideline, a summary is presented in Figure 1.

**Table 1.** Suggested laboratory investigations in the patients with coma.

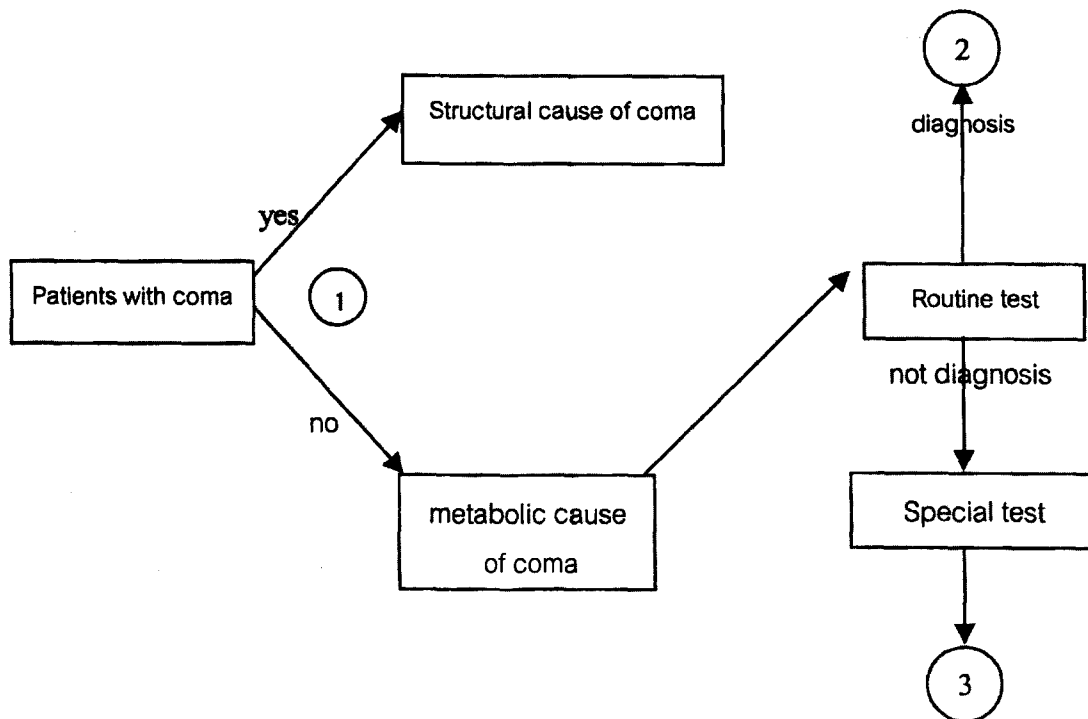
Groups	Tests
Routine test	Glucose, Electrolytes (Na, K, Cl, HCO <sub>3</sub> , Anion Gap), Calcium and Magnesium, Renal function (Creatinine, urea), Liver function (Bilirubin, AST), Urinalysis (glucose, ketones, specific gravity), Blood gas, Osmolarity*
Special test	CSF analysis (cell counts, color, protein, glucose, microbiology), Serum and urine for drug analysis (ethanol, salicylates, acetaminophen, opiate, tricyclic antidepressant)

\* can be both directly measured or calculated by the formula "Calculated osmolarity = 2 X [Na] + [urea] + [glucose] + [ethanol]"

1 = specific localized neurological sign and symptoms

2 = metabolic causes of coma due to metabolic disturbances or major organ failure

3 = metabolic causes of coma due to drugs



**Figure 1.** Laboratory guideline for diagnosis of the patients presenting with coma and unconsciousness.

1 = specific localized neurological sign and symptoms

2 = metabolic causes of coma due to metabolic disturbances or major organ failure

3 = metabolic causes of coma due to drugs

## Conclusion

In the patients presenting with coma and unconsciousness, laboratory investigations have important roles in the diagnosis. Many metabolic causes of coma can be definitely diagnosed by laboratory tests. A simple practical guideline is also given in this article.

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