The coma profile

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The comatose patient presents an urgent and challenging diagnostic and therapeutic problem for the clinician. From our experience, a cooperative effort between the clinical laboratory staff and the physician has evolved a diagnostic protocol which minimizes many of the pitfalls in the management of a patient in unexplained coma.

After examining the comatose patient, the physician requests the attending nurse to order a "coma profile" in which a large series of tests are performed on a "stat" basis. The physician fills in the coma profile form (*Table 1*) while samples of blood, urine, gastric contents, and spinal fluid (when indicated) are promptly drawn. One medical technologist is responsible for distributing samples and gathering data, thus minimizing the chance of losing samples and misplacing results. During the analyses, any abnormal findings are telephoned to the nurse-in-charge. The entire coma profile is returned to the chart within 1½ hours.

Our selection of tests which comprise the "coma profile" is by no means complete and can be easily modified. The SMA-12 provides rapid determinations of serum cholesterol, calcium, phosphorus, bilirubin, albumin, total protein, uric acid, BUN, glucose, LDH, alkaline phosphatase, and SGOT. Determinations of serum electrolytes

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Table 1. Coma profile form, Cleveland Clinic Department of Biological Chemistry

Name_____ Age_____ Sex_____ Clinic No._____

Answer if known:

1. How long in coma? ____ hours.
2. History of injury, ingestion, or known disease.
3. Send ingested drug(s) when available.
4. Pupillary size and light reflex _____.
5. Clinical impression:

All tests are performed STAT. Collect the following:

1. Clotted blood—30 ml.
   Oxalated blood—5 ml.
   EDTA blood—24 ml.
   Heparinized arterial blood—5 ml (leave in syringe).
2. Spinal fluid—4 ml (when indicated).
3. Gastric contents.
4. Catheterized urine specimen.

Call laboratory, Ext. 698. Samples will be picked up and distributed promptly. All abnormal data will be in red ink.

Signed: Dr. _____

Please call results to _____ as soon as possible. This test may be performed on patients in coma or impending coma of *undetermined etiology*.

(potassium, sodium, chloride, CO_2) and creatinine are also done on an autoanalyzer. Blood gases, serum acetone, cortisol, T-4, salicylate, and alcohol levels are often key factors in determining appropriate therapy. Spinal fluid testing should include both routine analysis and cytologic examination for atypical cells compatible with malignancy. Routine urinalysis is performed, and blood and urine specimens and gastric contents are examined for toxic substances. Blood cultures are obtained for microbiological analysis, and hematologic tests are rapidly performed on the Coulter Model S.

Admittedly, this program is open to criticism. First, it places a heavy work burden on laboratory personnel, especially at night and on the weekend when the number of staff is limited. The second point of possible criticism suggests that a sweeping "shotgun" type of survey conflicts with traditional medical practice, in which the physician orders only those tests he believes are indicated. Yet, it has been our experience that if the first small series of test results are noncontributory, then a second series of tests which may also be normal must be performed. Both the physician and, more importantly, the patient are losing crucial time under life-threatening circumstances. Our data suggest that it is more advantageous to perform approximately 25 tests on a "stat" basis and to expect a large percentage of normal results in order to obtain the unexpected abnormal result.

Increased availability and use of drugs has created a new dimension in the evaluation and therapy of the patient with unexplained coma. The older spectrophotometric methods in toxicology are time-consuming, lack specificity, and are usually applicable only to a single drug at a time.[1-3] Since 1969 the use of gas chromatography in our laboratory has provided a fast, simple, accurate, and reproducible

method for toxicologic studies. The evolving pattern of drug abuse suggests that potentially suicidal patients intoxicate themselves with overdosage of several drugs at a single time.[4, 5] Gas chromatography affords the chemist an opportunity to screen for small amounts of multiple drug metabolites in 30 minutes. Our choice of drug standards includes methyprylon (Noludar), amobarbital (Amytal), glutethimide (Doriden), pentobarbital, secobarbital (Seconal), chlorpromazine (Thorazine), phenobarbital, and diazepam (Valium). All these medications are commonly abused and overdosage is potentially fatal. Other drugs, such as amphetamines, heroin, meprobamate, chlordiazepoxide, and cocaine may be added to the series, if desired.

Whole blood is extracted with chloroform, dried with nitrogen gas, and one microliter is injected into a dual column Varian 2100 gas chromatograph. The carrier gas medium is nitrogen with a constant flow rate of 40 cc per minute. The oven temperature is kept constant at 235 C. The injection port is maintained at 270 C to instantly vaporize liquid samples. The separation process takes place in a 10-foot U-shaped glass tube containing a supporting material of diatomaceous earth (Chromosorb) which is packed with a nonpolar liquid known as High Efficiency 8 BP.* A flame ionization detector measures the components of the mixture in the column and transmits the impulse to a paper strip recorder. The same drug always behaves predictably under uniform extraction procedures, use of a standard column, specific temperature, and constant gas flow. Under these circumstances, a drug appears at the detector after a uniform time interval known as the retention time. The entire analysis can be performed within 30 minutes, and the instrument is available and in operating condition on a 24-hour basis.

We reviewed 124 case histories in which a coma profile was ordered for unconscious patients. Forty-two of these patients were comatose due to heart, lung, liver, kidney, endocrine, or nervous system disease, and toxicology studies were included solely for the sake of completeness. All 42 serum samples were negative by gas chromatography. Of the remaining 82 comatose patients suspected of drug intoxication, gas chromatography readily detected in 71 patients (87%) a serum, urine, or gastric level of one or a combination of drugs (*Table 2*). Of the remaining 11 patients with negative toxicology findings, two were later found to have carbon monoxide intoxication, five had alcoholic intoxication, two had cryptic head injuries, and in two the coma could not be explained by laboratory parameters. Simultaneous identification of a combination of drugs (as many as four in one patient) was obtained in 26 of 71 patients

Table 2. Frequency of coma profile drug types in 71 comatose patients by gas chromatography, Cleveland Clinic, 1969–1972

Drug	Percent
Secobarbital	35
Glutethimide	30
Pentobarbital	22
Amobarbital	10
Methyprylon	7
Phenobarbital	5
Chlorpromazine	2
Diazepam	1

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(32%). It is this ability to measure a variety of drugs in one small sample which makes gas chromatography especially applicable to clinical toxicology. Three patients with unidentifiable peaks on gas chromatography were later found to have ingested Sominex; ethchlorvynol (Placidyl); and carisoprodol, phenacetin, and caffeine (Soma Compound).

Secobarbital (a short-acting barbiturate) and glutethimide were the most commonly found drugs of abuse, with barbiturates in general and glutethimide noted to be agents of intoxication in more than 90% of the patients. We found that in 45 of 71 patients, histories obtained from families, friends, or physicians were not only noncontributory, but often misleading.

Thus far the discussion has been limited to qualitative rather than quantitative drug analysis. It has been our routine practice initially not to quantitate unknown drug levels. We feel that our main problem is *identification* of the toxic compound. Once the compounds are identified, extraction procedures may be modified to measure more accurately the specific

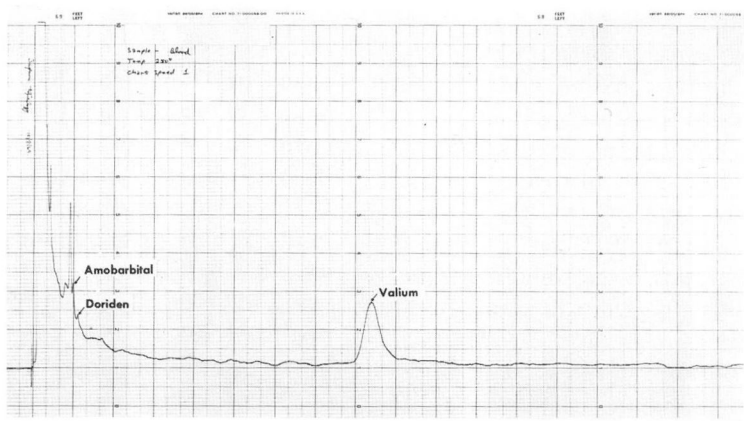

Fig. 1. Gas chromatograph of a blood sample from a comatose patient with diabetic ketoacidosis showed presence of amobarbitol, glutethimide (Doriden) and diazepam (Valium).

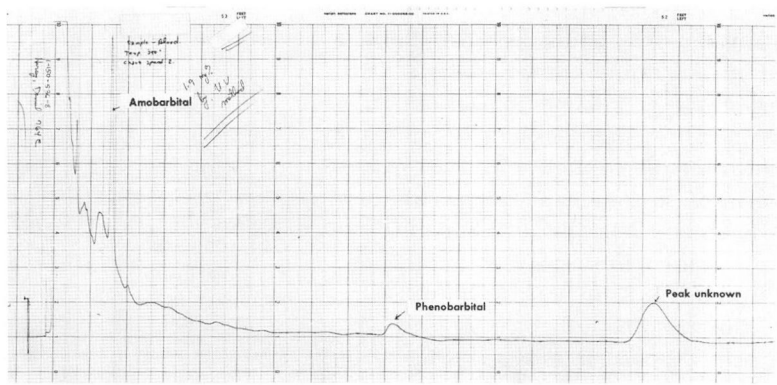

Fig. 2. Gas chromatograph of a blood sample from an epileptic child with coma of unknown etiology revealed unexpected and substantial amounts of amobarbitol and phenobarbitol.

drugs. Thus if chlorpromazine, an alkaloid tranquilizer, peaks on gas chromatography extraction may be done in alkaline medium at pH 11, and this second specimen is injected into the column. Serum peak area is then compared with the standard.

Gas chromatography has proved valuable in detecting the cause of coma. A known insulin-dependent diabetic man was admitted to our emergency room in acidotic coma with marked elevations of blood glucose and acetone and marked decrease in blood pH. Gas chromatography revealed blood levels of amobarbital, glutethimide, and diazepam (*Fig. 1*). The cause of death was probably ingestion of drugs, although the patient was admitted to the emergency room as a diabetic in coma. The gas chromatograph in *Figure 2* was done on a blood sample from a pediatric patient with a history of epileptic seizures. During hospitalization the patient mysteriously progressed into and out of coma, although no medication had been prescribed. Substantial amounts of amobarbital and phenobarbital were identified. When informed of these results, the mother admitted having given the child barbiturates on her visits to the hospital. Examples such as these reinforce our belief in the value of the additional work involved. We are occasionally confused by the presence of peaks with retention times other than our standards. These peaks may represent normal blood components such as palmitic acid, or they may represent drug compounds other than those we commonly encounter. Thus our method is not perfect. However, we have found gas chromatography to be an extremely useful adjunct in the determination of either single or multiple drug abuse.

In conclusion, we reemphasize the important role of the laboratory as an aid to the clinician who is confronted with the diagnostic and therapeutic parameters of the comatose patient. The coma profile is a series of tests designed to rapidly clarify the cause of unexplained coma.

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