has yielded correlations with active malignant disease (1, 3). However, the lack of specificity of changes in concentration of these components has decreased their clinical diagnostic usefulness.

By using cellulose acetate membranes with Mylar backing (4), we have been able to separate the α2-globulin region into several subregions. In Figure 1, we show the electropherogram of serum glycoproteins from a patient with increased acute-phase reactants. Adjacent to it is the pattern of a patient with metastatic ovarian adenocarcinoma, not responding to therapy. The observation that the acute-phase proteins migrate as a single α2 band is in contrast to the pattern of the cancer patient in relapse. In the latter, the α2 region consists of two subregions, which we designate “α2 slow” and “α2 fast” (4). We have observed this split pattern in a substantial number of adenocarcinoma patients with progressive, systemic disease, but in less than 5% of adenocarcinoma patients in remission or in patients with other types of malignancies or nonmalignant conditions. We find no evidence that increases in acute-phase proteins produce split α2 patterns. Thus, serum glycoprotein electrophoresis appears to be a feasible method for discriminating progressive disease in adenocarcinoma patients from nonspecific increases of α2-globulins. We agree with Ablin that any significant correlation between concentrations of α2-globulins in serum and tumor activity must be linked to specific measurements, or separation procedures such as electrophoresis.

References

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Increased Cerebrospinal Fluid Lactate and Early Diagnosis of Bacterial Meningitis

To the Editor:
Increased lactate concentrations in the cerebrospinal fluid (CSF) of patients suffering from bacterial meningitis were first noted in 1924 (1). However, only in recent years has its value in the early diagnosis of bacterial meningitis, as well as a differential aid in distinguishing this entity from viral meningitis, become recognized (2–4).

We have routinely measured CSF lactate for the past 18 months and have found it not only very helpful but also reliable. However, it is critical that the upper limit of normal be well established, to prevent confusion in some cases. In two relatively recent publications, normal limits were defined, but the numbers of fluids examined were much too few for any meaningful statistical evaluation and establishment of a reliable normal range (3, 4). Consequently, we have examined 161 consecutively obtained “normal” spinal fluids from children one day to 16 years old. Most, however, were younger than 2 years. Two slightly different enzymic methods were used, one a commercial kit (No. 826-UV; Sigma Chemical Co., St. Louis, MO 63178) and the other with in-house reagents essentially as previously described (5), except that perchloric acid rather than metaphosphoric acid was used. Both were determined with an Abbott Bichromatic Analyzer (ABA-50; Abbott Diagnostic Division, South Pasadena, CA 91030). Results by the two methods did not differ statistically. All fluids were colorless, clear, and contained fewer than 8 cells/mm³. Glucose and protein values were normal and bacterial cultures were negative.

A histogram (Figure 1) of the data shows skewing toward the higher values.

When the log of these values was plotted on normal probability paper, a straight line was obtained, indicating the data follow a log normal distribution. Calculations from the raw data, with use of log values, gave a mean of 159 mg/L (1.77 mmol/L) and a normal range of 100 to 253 mg/L (1.11–2.81 mmol/L). We have found this range to be completely reliable. We believe values of 250–300 mg/L should be considered borderline because an occasional apparently normal fluid yields values in this range. In addition, lactate concentration in viral meningitis also occasionally fall within this range (3), but most will be clearly below it. In essentially all bacterial infections, the value will exceed 300 mg/L, with only data on unusual early cases falling in the equivocal zone. We have yet to see a normal lactate value in a culture-proven case of bacterial meningitis, an observation in agreement with others (4), although this has been rarely noted (3).

We have, on occasion, received xanthochromic fluid for lactate analysis. These have invariably given high values, have no specific diagnostic significance, and should probably not be analyzed for lactate. In addition, one must keep in mind that the increase in lactate is apparently caused by tissue hypoxia owing to increased intracranial pressure with resulting impairment of the central blood supply (6, 7), and not by the destruction of bacteria by neutrophil leukocytes. Hence, increased CNS lactate concentrations are seen in brain tumors and other non-infectious conditions. It also explains why they are increased in tuberculous meningitis, where mononuclear cells usually predominate and microorganisms are few. In short, increased lactate concentrations are only of specific diagnostic value when interpreted in the appropriate clinical setting. When this is done, they are both helpful and reliable.

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References


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Intrauterine Growth Retardation and Catecholamine Metabolites in Amniotic Fluid

To the Editor:
Recently we reported the possible usefulness of determining catecholamine metabolites in amniotic fluid as an aid in the diagnosis of intrauterine growth retardation (1). This suggestion was based on the relatively low concentrations of free 3-methoxy-4-hydroxyphenylactic acid (HVA) in the amniotic fluid of three women who gave birth to small-for-dates babies (birth weight below 2.3rd centile).

Here we report the results of a more detailed study on this subject, including the amniotic fluid of 21 control patients and 20 patients who gave birth to small-for-dates babies. Controls and patients were selected on the basis of birthweights above and below the 10th centile, respectively. There were no significant differences between these groups with respect to the variables shown in Table 1, or related to parity, race, sex of newborns, renal diseases, diabetes, epilepsy, hypertension, cholestasis of pregnancy, Rhesus sensitization, pre-eclampsia, placental infarction, medications (corticosteroids, allylestrenol, ritodrine), or diastolic blood-pressure before and after delivery.

Table 2 shows results of measurements obtained for the amniotic fluid of controls and patients. We found no significant differences between the concentrations of homovanillic acid (free and total), vanilmandelic acid, 3-methoxy-4-hydroxyphenylglycol (free and total), creatinine, and the percentages of conjugated homovanillic acid and 3-methoxy-4-hydroxyphenylglycol. Even when the results obtained from women who gave birth to babies with birthweights below the 2.3rd centile were considered separately (five subjects), no significant differences could be demonstrated. We conclude that, despite the observation that the adrenal gland is one of the most growth-retarded organs during underdevelopment (2), there is no difference in total catecholamine turnover between growth-related fetuses and controls around the time of delivery. Furthermore, there is no difference in the conjugating capacity for these compounds.

Table 1. Some Variables Concerning Controls and Patients

<table>
<thead>
<tr>
<th>Control patients</th>
<th>Other patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. subjects</td>
<td>21</td>
</tr>
<tr>
<td>Age at admittance, y</td>
<td>27.8 ± 6.0</td>
</tr>
<tr>
<td>Gestational age</td>
<td></td>
</tr>
<tr>
<td>At amniocentesis, weeks</td>
<td>37.7 ± 1.9</td>
</tr>
<tr>
<td>At the time of delivery</td>
<td>39.4 ± 1.3</td>
</tr>
</tbody>
</table>

* ± values are SD.

Table 2. Catecholamine Metabolite Concentrations in the Amniotic Fluid of Controls and Patients Who Gave Birth to Small-for-dates Babies

<table>
<thead>
<tr>
<th>Compound</th>
<th>Control patients (n = 21)</th>
<th>Other patients (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x ± SD Range</td>
<td>x ± SD Range</td>
</tr>
<tr>
<td>HVA free</td>
<td>8.24 ± 1.76 5.56-11.72</td>
<td>7.68 ± 1.50 5.65-10.88</td>
</tr>
<tr>
<td>total</td>
<td>10.74 ± 2.86 6.18-15.23</td>
<td>9.88 ± 1.79 7.51-14.32</td>
</tr>
<tr>
<td>VMA</td>
<td>6.08 ± 1.25 4.46-9.48</td>
<td>6.10 ± 1.34 3.67-8.79</td>
</tr>
<tr>
<td>MOPEG free</td>
<td>1.56 ± 0.49 0.59-2.61</td>
<td>1.74 ± 0.54 0.98-2.72</td>
</tr>
<tr>
<td>total</td>
<td>3.86 ± 0.88 2.85-6.20</td>
<td>3.66 ± 0.90 2.50-6.30</td>
</tr>
<tr>
<td>Creatinine</td>
<td>14.9 ± 4.9 8.5-27.1</td>
<td>17.0 ± 4.7 8.5-26.0</td>
</tr>
<tr>
<td>HVA conj.</td>
<td>23.8 ± 8.5 6.5-37.6</td>
<td>21.7 ± 11.0 2.5-42.4</td>
</tr>
<tr>
<td>MOPEG conj.</td>
<td>59.3 ± 11.3 38.5-81.4</td>
<td>51.4 ± 13.4 27.7-78.1</td>
</tr>
</tbody>
</table>

n, no. subjects; conj., conjugated; HVA, homovanillic acid; VMA, vanilmandelic acid; MOPEG, 3-methoxy-4-hydroxyphenylglycol. * mg/g creatinine. # mg per liter. % percentage.

References


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Serum Anticonvulsant Monitoring by Liquid Chromatography with a Methanolic Mobile Phase

To the Editor:
"High-pressure" liquid chromatography has become a powerful tool for monitoring drugs in serum. However, published methods for the simultaneous determination of anticonvulsants (1-4) and other sedative and hypnotic drugs (5) by reversed-phase liquid chromatography have used relatively expensive and toxic acetonitrile as the organic component of the mobile phase. We report our initial experience with a methanolic mobile phase, used mainly for monitoring anticonvulsants in serum but also for drug screening.

The procedure was developed on the Hewlett-Packard 1084A, dual pump, programmable liquid chromatograph with a C-18 reversed-phase column (Brownlee Labs., Santa Clara, CA 95050) protected by a Whatman guard column containing CoPell ODS packing.