3 Diagnostic Procedures: Function Tests and Postmortem Protocol

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3.1 Introduction

Functional investigations are based on the measurement of intermediary metabolites in body fluids. They are most useful in disorders that give rise to toxicity or energy deficiency. The best functional test is elicited by nature itself during episodes that cause metabolic stress, including acute infection, inadvertent fasting, or consumption of a nutrient that induces a metabolic intolerance. If an inherited metabolic disease is suspected then blood, urine and cerebrospinal fluid should be collected for the appropriate investigations (Table 1.3). If no material is available or if the results are ambiguous, a provocative test that challenges a metabolic pathway may provide clues for a diagnosis and indicate which specific enzymatic or genetic analysis should be undertaken.

When performing a functional test, it is important to adhere to a strictly defined protocol in order to attain a maximum of interpretable diagnostic information and to minimize the risk of metabolic complications. Some of the tests described in this chapter are now used infrequently, since more simple direct assays of metabolites and DNA have reduced their diagnostic value. This applies to the galactose, fructose, or fat-loading tests. Other tests have fallen into total disuse and are not considered here. These include the glucagon test for the differentiation of glycogen-storage diseases and the phenylpropionate loading test for diagnosis of medium-chain acyl-coenzyme A dehydrogenase deficiency.

3.2 Functional Tests

3.2.1 Metabolic Profile over the Course of the Day

Indications

This first line of evaluation of intermediary metabolism may be performed following an initial or recurrent clinical incident associated with a disturbance of intermediary metabolism in which the aetiology is unknown. The investigation is useful in the metabolic/endocrine investigation of hypoglycaemia, hyperlactatemia, hyperketosis or hypoketosis and, in these situations, should always be undertaken before any provocative test that may lead to metabolic decompensation. The metabolic profile is also used for monitoring treatment in many disorders.

Procedure

Blood samples from an indwelling venous catheter (kept patent with a saline infusion) are taken before and after meals, and once during the night, as outlined in Table 3.1.

### Table 3.1. Assessment of intermediary metabolism over the course of the day

<table>
<thead>
<tr>
<th>Parameters in blood</th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Dinner</th>
<th>Night</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>1 h after</td>
<td>Before</td>
<td>1 h after</td>
</tr>
<tr>
<td>Glucose^1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Acid-base</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate^2</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pyruvate^2</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Free fatty acids</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ketone bodies</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ammonia</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Amino acids</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carnitine</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acylcarnitines</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormones^3</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Urine 24 h collection^4 Amino acids, organic acids, ketone bodies, urea, creatinine

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^1 Glucose should be determined immediately.

^2 Immediate deproteinization (with perchloric acid) at the bedside is the only way of ensuring that the results for calculating redox potential ratios can be accurately interpreted.

^3 Hormones (insulinemia, cortisol, growth hormone) are useful in the investigation of hypoglycaemia.

^4 Urine samples are collected both overnight and during the day and should be frozen immediately.