1.4.1 Introduction

Lactate, pyruvate, acetoacetate (ACAC) and 3-hydroxybutyrate (3OHB) are intermediary metabolites that normally occur in blood and play an essential role in energy production. Their accumulation in blood is a frequent cause of metabolic acidosis in children. The determination of these metabolites in biological fluids is useful in the early detection, diagnosis and treatment follow-up of abnormalities such as those of:

1. Enzymes of pyruvate “metabolism” (pyruvate dehydrogenase, PDH, or pyruvate carboxylase, PC, defects).
2. Enzymes of the Krebs cycle.
3. Enzymes of gluconeogenesis.
4. Liver glycogenolysis.
5. Oxidation of fatty acids.
7. Mitochondrial respiratory chain.

Their relative blood concentrations are an expression of nutritional balance, providing a view of the metabolic disturbances arising in a patient. In conjunction with the measurement of unesterified fatty acids (UEFA) and glucose, they are useful tools with which to investigate intermediary metabolism in health and disease, particularly in inherited metabolic diseases.

During fasting, hormonal or metabolic modifications mobilise energy stored in adipose tissue as fat. Evaluation of different metabolite concentrations in blood provides insight into the different steps of fat metabolism.

Determinations of lactate, pyruvate, 3OHB and ACAC in biological fluids are run at different times during the day according to different periods of fasting. They are usually performed before and after meals (1 h). They are also performed after loading tests (e.g. glucose, proteins or triglycerides.)

1.4.2 Properties of Analytes

The plasma lactate (CH$_3$-CHOH-COOH) levels reflect the equilibrium between its production and its consumption by different tissues. Lactate is the end product of
anaerobic glycolysis, which is the main energy source for tissues such as the heart, muscles and kidney. Accumulation of lactate in blood to levels higher than 7 mmol/l leads to lactic acidosis. Hyperlactataemia can be observed either in ischaemic conditions or in many inherited metabolic diseases (e.g. PDH deficiency, PC deficiency).

During fasting, lactate is used by the liver and kidneys to provide glucose (gluconeogenesis). Blood lactate decreases during the first 15 h of fast (about 30% regardless of age). In the postprandial period, lactate is oxidised in mitochondria, producing energy for the heart, muscles and kidneys. The different metabolic pathways of pyruvate and lactate interconversion are shown in Fig. 1.4.1. The ratio of lactate to pyruvate remains unchanged independent of the fasting state.

Lactate and pyruvate are interconverted within the cytoplasm, depending upon the NAD:NADH ratio. In the cytoplasm, the ratio of lactate to pyruvate reflects the oxidoreduction state.

Pyruvate (CH$_3$-CO-COOH) is an intermediate metabolite, the product of carbohydrate, fat or protein metabolism. Pyruvate is the end point of glycolysis. In mitochondria, pyruvate may be oxidized to CO$_2$ and H$_2$O, reduced to acetyl coenzyme A (acetyl CoA) by PDH, or carboxylated by PC into oxaloacetate (Fig. 1.4.2).

![Lactate and pyruvate metabolic pathway](image_url)

**Fig. 1.4.1** Lactate and pyruvate metabolic pathway. (P Phosphate, PEP phosphoenolpyruvate)