

## LACTATE DEHYDROGENASE

**W**e will analyse in this fourth Bulletin on the interference of drugs in clinical trials the effects that the most important compounds interfering with Lactate Dehydrogenase, LDH, testing cause.

This enzyme has a tetrameric quaternary structure, resulting from the combination of the H or M monomers, which receive their denomination from the prevalent location either in the Heart or the Muscle. LDH is widely distributed in the cellular cytoplasm in almost all tissues, although its presence is especially relevant in liver cells. LDH concentrations in tissues are about 500 times higher than in surrounding serum, and so even small cellular lesions can mean the release of the enzyme and significantly increase the plasma concentration. One of the main "interference" effects of the drugs is to provoke liver injury and artificially increase the serum concentration of a typical cytoplasmic component, such as is the case with LDH.

### CLINICAL MEANING

Lactate Dehydrogenase is present in all cells in the body although the main concentrations are found in the liver, heart, kidneys, skeletal muscle and erythrocytes.

High serum levels of LDH are reported in many circumstances. High levels (increases from 2 to 40 times the normal value) are seen in the case of megaloblastic anemia, in extensive carcinomatosis, in serious shock and in anoxia. Moderate increases (from 2 to 4 times) occur in myocardium infarct, lung infarct, granulocytic or acute leukemia, hemolytic anemia, infectious mononucleosis and progressive muscular dystrophy patients. Slight relative elevations occur in cases of hepatitis, obstructive jaundice or cirrhosis, yet much higher values are given in delirium tremens. Patients with chronic nephropathy, especially with nephrotic syndrome or with hemolytic anemia also have high values. LDH values also increase in myxedema, presumably because of muscular alterations.

The large number of circumstances in which increased LDH are observed dissipates somewhat the diagnostic use of its quantification. The LDH value is clinically useful in diagnosing myocardium and lung infarcts. It is also useful in extensive carcinomatosis since it is used as a guide in a course of cancerous chemotherapy, since the therapeutic response is frequently reflected by a decrease of serum enzymes.



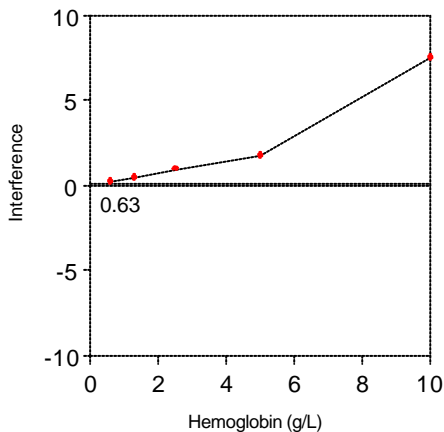
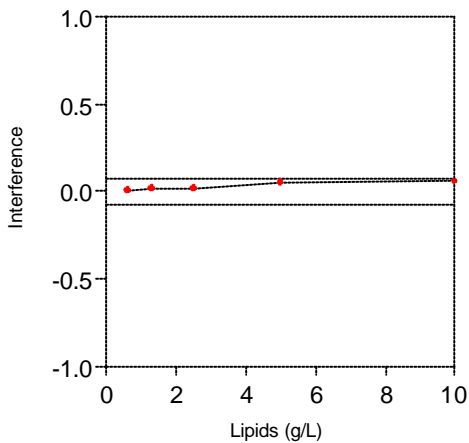
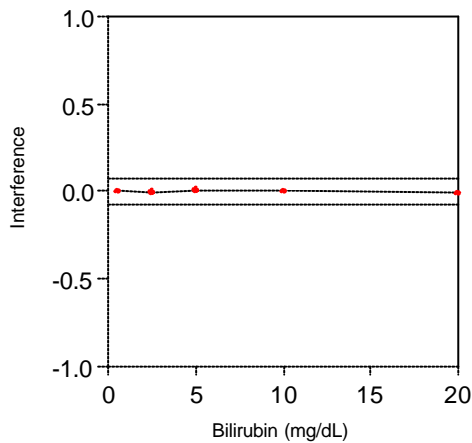
## METHODOLOGY INTERFERENCES

*Pyruvate-Lactate, Lactate-Pyruvate (IFCC)*

Each point is the average of three. Horizontal lines show the tolerance for the value obtained in the presence of interferent, calculated as: the average in the absence of interferent  $\pm 3 \times$  between runs standard deviation.

Sample: human serum without (a) and with growing concentrations of interferent (b).

Interference:  $(b-a)/a$



Hemolysis interferes due to the high lactate dehydrogenase concentration in red blood cells.

Lipemia (triglycerides  $< 10$  g/L) and bilirubin ( $< 20$  mg/dL) do not interfere.

## DRUG INTERFERENCES

### ANALYTICAL INTERFERENCES (DECREASE)

#### ACETYLSALICYLIC ACID

Concentrations higher than  $8.3$  mmol/L decrease the serum concentration of LDH in methods which use pyruvate as a substrate.

#### DIPYRONE

In vitro interferences reported at a concentration of  $44$   $\mu\text{mol/L}$ . 16% enzyme activity reduction when 2 grams administered intravenously after 2 minutes and 5% after 60 minutes.

#### METRONIDAZOL

This drug interferes with enzymatic tests (even giving 0 values) in which case the method of coupled reactions using NAD/NADH at 340 nm was used.

### PHYSIOLOGICAL INTERFERENCES (DECREASE)

#### ANTICONVULSANTS

Average concentration of  $144.8 \pm 4.6$  U/L reported with regard to the basal concentration of the control group,  $161.6 \pm 6.0$  U/L, in 99 epileptic patients when administered.

#### ENALAPRIL

Significant reduction reported in 27 hypertense patients when a dosage of 2.5 mg/day administered for more than 3 months. Average concentration passed from 333 U/L to 207 U/L when administered.

#### NALTREXONE

Significant serum LDH concentration decrease reported in 53 patients when administered for 3 months.



## **PHYSIOLOGICAL SERUM INTERFERENCES (INCREASE)**

### *VALPROIC ACID*

Non significant serum LDH concentration increase when administered. The increase is dosage dependent.

### *ANESTHESIAS*

Serum LDH concentration increase reported even when premedicating patients.

### *CAPTOPRIL*

Serum concentration increase because of cholestasis and hepatocellular jaundice reported when administered.

### *CEFTAZIDIME*

Concentration increase reported when administered during clinical trials was medium and transitory. Normally reported in 1 of every 18 patients (5.5%).

### *CEFUROXIME*

Transitory increases reported in 2% of patients when administered.

### *ANABOLIC STEROIDS*

Normally occurs as a consequence of a cholestatic syndrome.

### *ESTRAMUSTINE*

When administered to patients it is normal to observe alterations in the hepatic function tests, such as Bilirubin, AST and LDH.

### *GRANULOCYTE COLONY-STIMULATING FACTOR (G-CSF)*

Significant increase (27 – 58% of patients) reported of serum LDH concentration when administered.

### *HYDRALAZINE*

Reversible serum LDH concentration increase when administered.

### *INTERFERON $\alpha$ 2a*

When administered there is an LDH activity increase between 1-10% depending on pathology type.

### *INTERLEUKIN-2*

80% LDH activity increase reported in 21 cancer patients when administered for 5 days.

### *LEVODOPA*

LDH activity increase associated when administered but the reason unknown.

### *NORFLOXACIN*

Significant LDH activity increase reported in 1% of patients with urinary tract infections or prostatitis when administered.

### *PENICILLAMINE*

LDH activity increase as a result of toxic hepatic necrosis in 6 of 99 patients when administered.

### *QUINIDINE*

Isolated cases of LDH increase when administered.

### *TICARCILLIN*

LDH activity increase in some patients receiving this drug and Clavulanate but rare appearance of transitory hepatitis or cholestatic jaundice as with other penicillins and some cephalosporins.

## **NON INTERFERING DRUGS**

The following drugs do not interfere at therapeutic concentrations:

Acetylsalicylic Acid, Alopurinol, Ampicillin, Barbitol, Bromazepam, Cefotaxime, Chloramphenicol, Codeine, Diazepam, Digitoxine, Phenobarbital, Flurazepam, Gentamicin, Ibuprofene, Isoniazid, Lidocaine, Mercaptopurine, Methimazole, Morphine, Naproxen, Piperacillin, Quinine, Rifampicine and Salicylate.



**BioSystems**

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Costa Brava 30, 08030 Barcelona (Spain) Tel. +34-93 311 00 00 Fax +34-93 346 77 99  
e-mail: biosystems@biosystems.es <http://www.biosystems-sa.com>