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ST VINCENT'S PATHOLOGY

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ALKALINE PHOSPHATASE (ALP) INFORMATION SHEET

GENERAL

The alkaline phosphatases (ALP) are a group of enzymes with similar catalytic activity. They may be found in high concentration in several tissues throughout the body. Different tissues contain different isoenzymes or isoforms, and this may allow identification of the source of ALP in some cases. The tissues which contain highest amounts of ALP are liver, bone, placenta, and intestine. As a liver function test ALP particularly reflects pathology of the biliary system and is therefore sometimes known as a "cholestatic enzyme". In this setting GGT is also commonly elevated.

HIGH LEVELS OF ALP IN PLASMA

High circulating levels of ALP may be caused by physiological or pathological changes. The most common tissue sources for pathological elevations are bone and liver. In all cases ALP elevation is due to increased production with induction of ALP formation. This is in distinction to the transaminases which are found in elevated concentrations in the serum because of release from damaged cells.

PHYSIOLOGICAL RISES IN ALP (source in brackets)

- Any period of growth, especially infants and during adolescence (bone)
- During pregnancy, especially during the third trimester (placenta)

PATHOLOGICAL RISES IN ALP DUE TO BONE DISEASE

- Paget's disease
- Bone malignancy (primary or secondary)
- Hyperparathyroidism
- Vitamin D deficiency
- Healing fracture
- Chronic kidney disease (CKD)

ALP is a marker of bone formation due to osteoblast activity. GGT is commonly not elevated in these conditions.

PATHOLOGICAL RISES IN ALP DUE TO LIVER DISEASE (hepatic)

- Cholestasis, including inflammation of the biliary tree
- Hepatocellular damage – less significant and delayed compared to the rise in ALT
- Hepatic space occupying lesion, including primary or secondary malignancies
- Drugs, especially alcohol and anti-convulsants (less frequently than GGT)

GGT is commonly also elevated in these conditions.

OTHER CAUSES OF ALP ELEVATION

- Ectopic production by malignancies – the Regan isoenzyme
- Transient hyperphosphatasaemia of infancy
- Hyperthyroidism
- Congestive cardiac failure
- Macro-ALP (ALP- immunoglobulin complex, very rare)

ALKALINE PHOSPHATASE ISOENZYMES

PHYSIOLOGY: There are 4 genes in the ALP gene family: intestinal (found on chromosome 2); placental (2); germ cell (2) and non-tissue specific (1). The tissue non-specific isoenzyme includes the common serum forms of ALP from bone and liver.

Intestinal and placental are "true" isoenzymes, ie from different genes. Liver and bone ALP are isoforms of the tissue non-specific isoenzyme, differing due to post-translational glycation. In adult plasma bone and liver ALP are found at similar concentrations. In children bone ALP is usually the predominant form in the circulation. Bone ALP is an ectozyme of osteoblasts bound to outer cell membranes by linkage to phosphotidyl inositol, some of which is released into the circulation.

PATHOLOGY: Circulating levels of bone ALP are raised in conditions of increased bone deposition, ie increased osteoblast activity. This occurs during bone growth (eg puberty), with various diseases and some drugs (eg cyclosporin treatment). Low levels occur with decreased bone deposition (eg systemic steroid treatment). Serum concentrations of bone ALP parallel growth velocity and may be used to monitor the response to Growth Hormone treatment in children. Placental ALP is found in the circulation during pregnancy and is identified by a marked stability to heating. This type of ALP is also occasionally produced by malignancies.

MEASUREMENT: In most cases the source of the ALP is not in doubt. Comparison with GGT is generally informative with simultaneous rises occurring when liver is the source and ALP alone with bone sources. Qualitative identification may be performed by several techniques of which electrophoresis is the most used method. Results from this method will indicate the predominant form present in the plasma and the presence of any abnormal forms. The method however is not quantitative. It is not possible to perform fractionation at total ALP concentrations of less than 150 U/L.