

## P III P

- Determination of N-terminal procollagen-III-peptide
- The fibrosis marker in liver diseases

# P III P

Reference : OCFK07 – PIIP

## Biochemistry

### Biochemical principles

Collagen is the major constituent of the extracellular matrix of connective tissue and accounts for approximately 30% of total protein in the body.

Type III collagen occurs principally in reticular connective tissue, parenchymatous organs, vessels and, in small quantities, in the skin. Initially, procollagen III is synthesized by the cell and secreted into the extracellular space. The propeptides then undergo cleavage.

The amount of cleaved propeptide (procollagen-III-peptide, P III P) is therefore a direct index of the amount of collagen synthesized and deposited in the extracellular space.

While the resultant collagen monomers are deposited in connective tissue as collagen fibrils, some of the propeptides enter the bloodstream and can therefore be detected in serum<sup>(6) (7)</sup>.

The N-terminal procollagen-III-peptide Col 1-3 (MW 45000) can be broken down by proteolysis into Col 1 (MW 10 000) (Figure 1).

Col 1-3 can be detected in serum using P III P (ref. OCFK07- P III P).

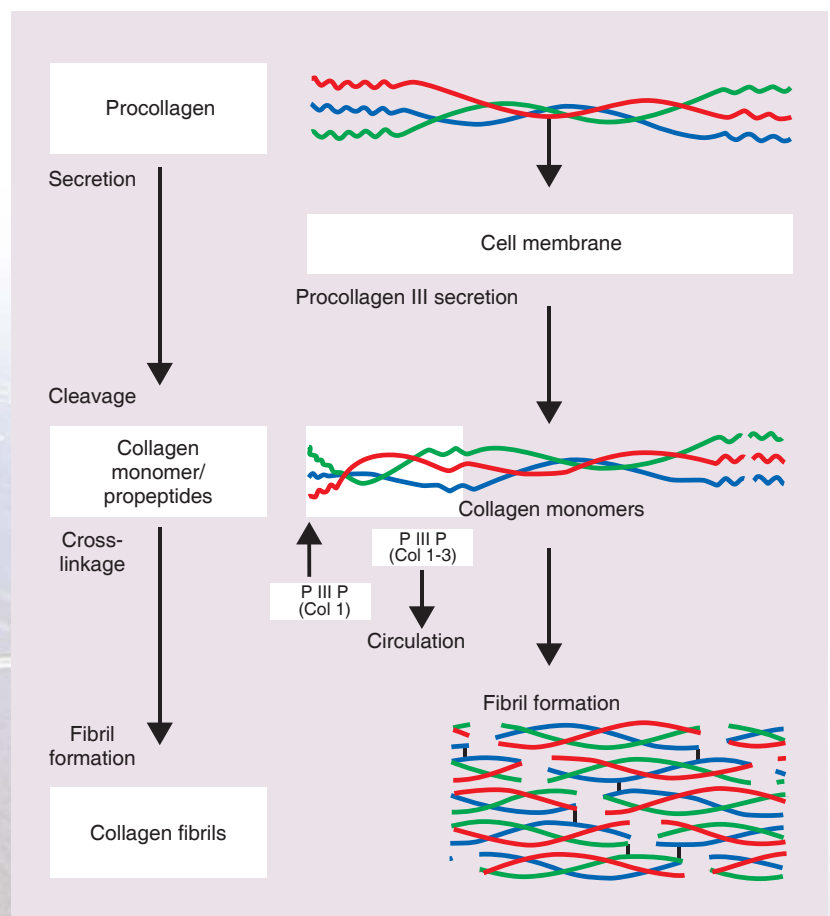


Figure 1 : Biosynthesis of procollagen-III-peptide

# Clinical aspects

## Clinical importance

In addition to minimal amounts of type IV collagen, the connective tissue of the liver principally contains collagen types I and III. The active proliferation of connective tissue (fibrosis) in the liver as a result of pathological situations (figure 2) is associated with the increased presence of procollagen-III-peptide Col 1-3, the concentrations of which can be determined in the serum<sup>(1) (4)</sup>.

Elevated serum concentrations of procollagen-III-peptide therefore point to the transformation of viable hepatic tissue into connective tissue. This is the case, for example, in alcohol-induced or viral hepatic fibrosis and cirrhosis. Raised procollagen-III-peptide levels are also encountered in certain other diseases, such as pulmonary fibrosis, and Paget's disease, chronic polyarthritis and collagenoses<sup>(2) (3) (9)</sup>.

## Normal range

In clinical trials, the normal range of procollagen-III-peptide in male and female sera was determined using PIIIP (figure 3). The median of 158 serum samples from the study group in women and men without liver disease was 0.53 U/ml. The 5<sup>th</sup> percentile was 0.33 U/ml and the 95<sup>th</sup> percentile was 0.79 U/ml.

The lowest measured value was 0.21 U/ml and the highest value was found at 0.98 U/ml.

Taking into account all admissible results from different centres, the normal range for serum concentration of procollagen-III-peptide extends from 0.3 to 0.8 U/ml.

The serum concentration of pro-collagen-III-peptide displays a clear physiological age-dependence in children.

Serum concentrations of procollagen-III-peptide fall continuously as the child grows older, with adult values being attained by the age of 20.

Elevated values are also found in pregnant women, but normal concentrations are restored within 8 weeks of childbirth.

## Indications for the assay of procollagen-III-peptide

For monitoring the evolution of liver diseases, e.g.

- Chronic active hepatitis
- Liver fibrosis
- Liver cirrhosis

Figure 2 : Indications for RIA-gnost® P III P

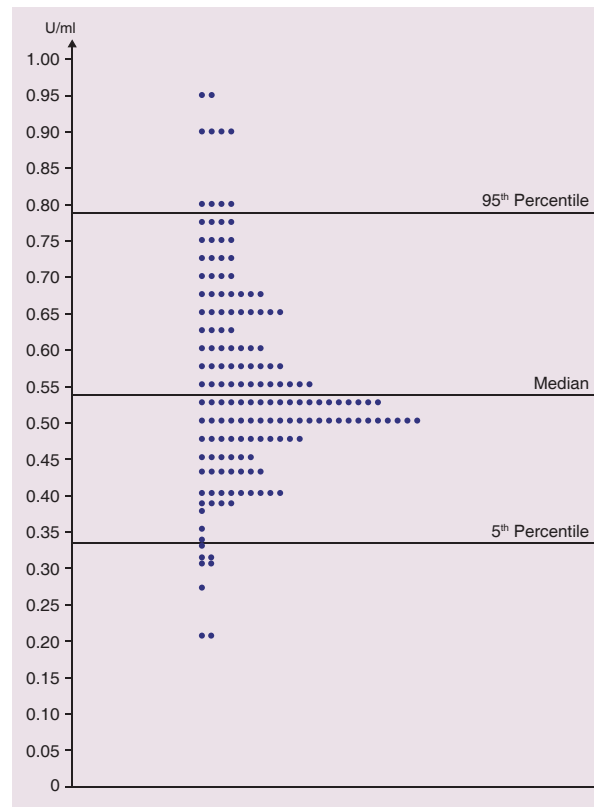


Figure 3 : Normal range for RIA-gnost® P III P

Note: to convert U/ml into µg/L, multiply the results obtained with the Cisbio kit by a factor of 8.

Example: 0.53 U/ml = 8 x 0.53 = 4.24 µg/L

### P III P in liver diseases

Pathological situations involving the liver and associated with active proliferation of connective tissue are characterized by elevated serum concentrations of procollagen-III-peptide.

The transformation of viable hepatic tissue into connective tissue is thus reflected in the procollagen-III-peptide level.

The diagnostic importance of serum concentrations of procollagen-III-peptide in this context does not lie in initial diagnosis but in monitoring the disease evolution in order to quantify the existing degree of fibrosis (figure 4)<sup>(2) (3) (5) (8) (9)</sup>.

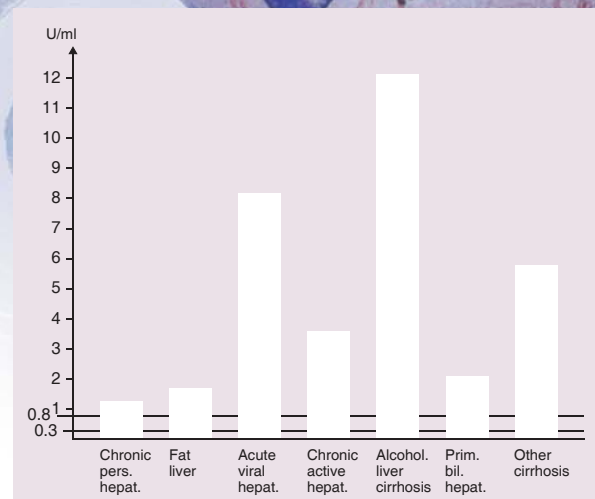


Figure 4 : RIA-gnost® P III P serum concentrations in various liver diseases

### Correlation of P III P and histological examination of the liver

A good correlation was obtained between serum procollagen-III-peptide concentrations and morphometry of portal field sizes in liver biopsy in a population of 50 patients with fibrotic liver disease.

In a sub-group of 29 patients, a minimum of 5 portal fields per biopsy permitted to morphometric assessment and their sizes were correlated with the serum procollagen-III-peptide concentrations.

The serum procollagen-III-peptide concentrations were determined from a blood sample drawn from the patients within 14 days of histological examination.

The correlation was  $r = 0.85$  (figure 5)<sup>(1)</sup>.

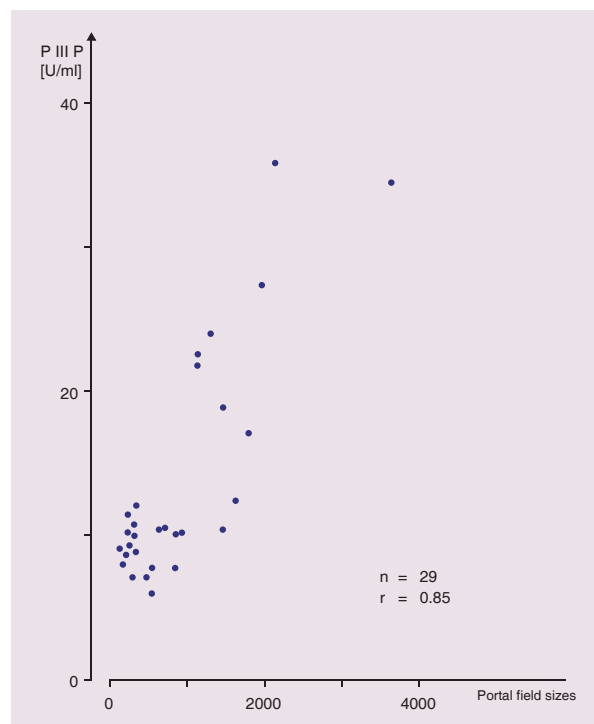


Figure 5 : RIA-gnost® P III P correlation with histological findings



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