



# Analysis of cytokines

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## FROM THE LABORATORY

### ELIN STORJORD

E-mail: [elin.storjord@gmail.com](mailto:elin.storjord@gmail.com)

Elin Storjord is a specialist in anaesthesiology and medical biochemistry, a senior consultant at the Department of Laboratory Medicine, Nordland Hospital and a PhD student at UiT The Arctic University of Norway.

The author has completed the ICMJE form and declares no conflicts of interest.

### LINDA TORRISSEN HENNØ

Linda Torrisen Hennø is a general practitioner at Alstad Medical Centre, Bodø.

The author has completed the ICMJE form and declares no conflicts of interest.

### TOM EIRIK MOLLNES

Tom Eirik Mollnes is a specialist in immunology and transfusion medicine, a research group leader at the Research Laboratory, Nordland Hospital, and a professor at UiT The Arctic University of Norway.

The author has completed the ICMJE form and declares no conflicts of interest.

### OLE-LARS BREKKE

Ole-Lars Brekke is a specialist in medical biochemistry, chief consultant of the Department of Laboratory Medicine, Nordland Hospital and a professor at UiT The Arctic University of Norway.

The author has completed the ICMJE form and declares no conflicts of interest.

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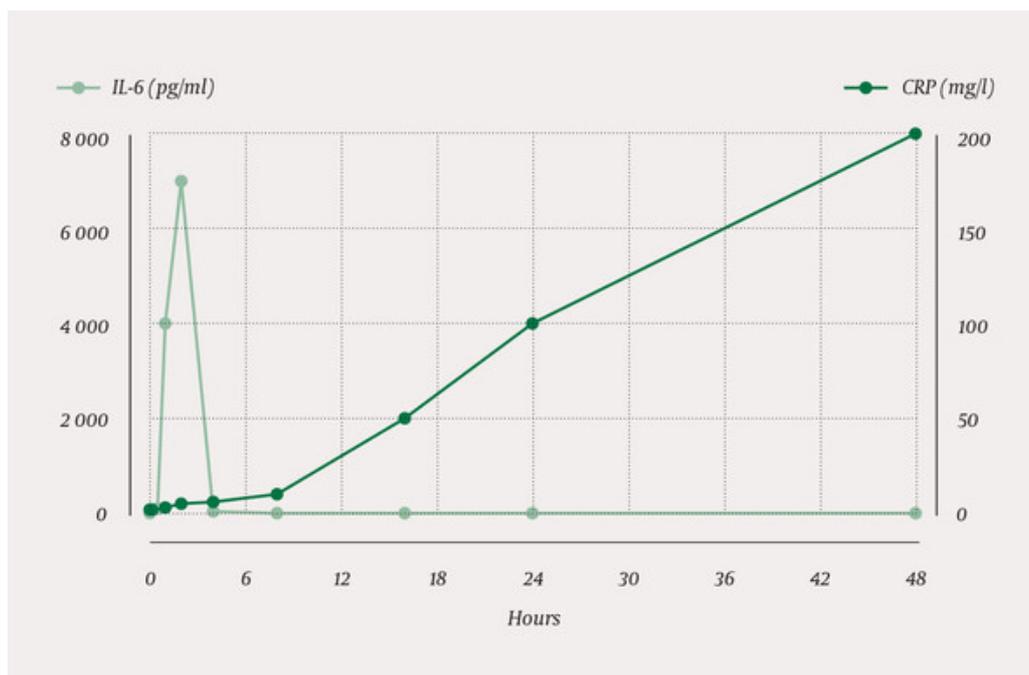
## Cytokines may become an important diagnostic tool in the future, but for the time being are mainly used in research.

Cytokines are small signalling proteins which include interleukins (IL), chemokines, interferons (IFN) and growth factors. Cytokines bind to cell receptors and regulate a number of immune responses that may be pro- or anti-inflammatory (1). Some classic examples of cytokines are tumour necrosis factor (TNF), IL-6, IL-1 $\beta$ , the chemokine CXCL8 (IL-8), IFN- $\alpha$ , - $\beta$  and - $\gamma$ , and the growth hormone granulocyte colony-stimulating factor (GCSF).

## Potential indications

Some patients lack a CRP response (2). Cytokines such as IL-6 may be a marker of the future in cases like this when bacterial infection is suspected in patients with cirrhosis of the liver (3).

CRP may have a lower sensitivity than IL-6 at the start of an infectious process (Fig. 1). For example, measuring IL-6 in the first 24 hours following a trauma may be useful for predicting post-traumatic complications such as multi-organ failure (4).



**Figure 1** Typical time course for concentration of the cytokine IL-6 and CRP in plasma in cases of acute inflammatory response. Fever peaks and falls in blood pressure coincide with the cytokine peak in cases of sepsis.

A number of studies of cytokines in connection with sepsis have been performed without any good diagnostic biomarker being found. However, it has been proposed using IL-6, IL-1 $\beta$  and TNF on suspicion of neonatal sepsis (5).

## Analysis

Many cytokines exhibit wide biological variation (1) and there may be circadian and seasonal variation (6). Cytokine levels are influenced by biological variables such as age, gender and body mass index, and environmental factors such as diet, microbiome and genetic factors (7).

Cytokine concentrations may increase substantially during illness. A number of different conditions such as sepsis, rejection reactions following transplantation, cardiovascular disease, cancer, rheumatic disorders, overweight, Alzheimer's disease, asthma, kidney damage, Parkinson's disease, depression (1) and diabetes with chronic periodontitis may result in increased cytokine levels (8).

There are still many challenges associated with the diagnostic and prognostic use of cytokines, including a number of analytical methods that are not standardised or directly comparable, and a lack of internationally established reference ranges for the various technologies. We recently published an article investigating optimal sampling conditions (9). It is especially important that whole blood is not left to stand before centrifuging, because it is the blood cells that produce and release cytokines after sampling. We recommend EDTA plasma as sampling material for measuring these cytokines. In the study, we calculated reference intervals for the 27 cytokines in EDTA plasma from 162 healthy individuals, analysed by means of multiplex immunoassay (9). In healthy individuals, many cytokines were either unmeasurable or detectable only in very low concentrations (1, 9).

## CONCLUSION

Cytokine assays are mainly used in research projects to explain cell biology mechanisms. Analysis of cytokines in plasma and other body fluids may be useful for clinical diagnostics in the future. More research linking the laboratory with clinical tests is necessary before a consensus can be reached on which cytokines, which levels and which cytokine patterns may be of significance for clinical diagnostics, treatment and prognosis for different pathological conditions.

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