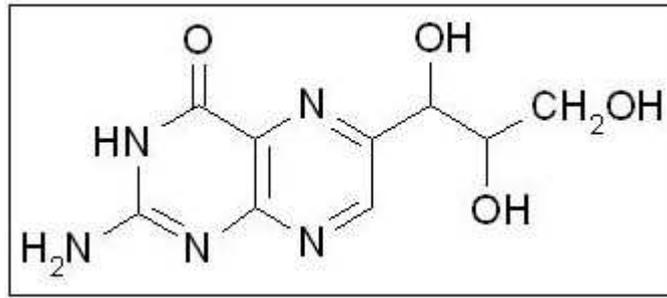


## Neopterin – in brief

(see also [www.neopterin.net](http://www.neopterin.net))



### Neopterin

(D-erythro-1'2'3'-Trihydroxypropylpterin)

Biochemically neopterin derives from guanosine triphosphate, and it is formed and released from human monocyte-derived macrophages and dendritic cells upon stimulation with the pro-inflammatory cytokine interferon- $\gamma$  [1]. Relevant concentrations of the low-molecular mass substance neopterin (molecular mass 253 Da) are detectable only in humans and primates. In agreement with the *in vitro* background, increased neopterin concentrations are commonly observed during diseases in which the cellular (Th1-type) immune system is involved. These include primarily infections with viruses and intracellular bacteria, autoimmune syndromes and malignancies, and allograft rejection episodes. Recent investigations show that neopterin derivatives are able to modulate and amplify effects of reactive oxygen metabolites, which are also released during the immune response. Thus, increased neopterin concentrations in patients demonstrate an activated cell-mediated (= Th1-type) immune system and the herewith connected development of oxidative stress [1-3].

### Clinical relevance

#### *Infections:*

Particularly high neopterin concentrations are observed in acute virus infections, but also during infections with intracellular pathogens, e.g., pulmonary tuberculosis and malaria, and the neopterin concentration is an independent predictor for the future course of disease and outcome in, e.g., patients with HIV-infection. Neopterin alone or even better in combination with C-reactive protein is very well suited to support the differential diagnosis of viral versus bacterial infections [4].

#### *Carcinoma:*

In patients with malignant tumors, neopterin concentrations correlate with the stage of the disease. Moreover, neopterin concentrations measured at diagnosis revealed independent prognostic information for the future disease course [5]. These include gynecologic and hematologic tumors as well as carcinoma of the lung, pancreas and stomach and malignant melanoma.

#### *Cardiovascular, neurodegenerative and other inflammatory diseases:*

Older age is often associated with increasing neopterin concentrations, whereby especially the development of atherosclerotic abnormalities and neurodegenerative disorders (e.g., *Morbus Alzheimer*) are associated with elevated neopterin concentrations. Recent investigations showed that the neopterin concentration is among the best prognostic parameters in patients with cardiovascular risks [6-8].

In autoimmune syndromes like rheumatoid arthritis or systemic *lupus erythematosus*, neopterin concentrations correlate with the extent and particularly with the activity of the disease, therapeutic effects are indicated rapidly.

#### *Screening of blood donations:*

To further reduce the infection risk of blood transfusion, every blood donation with an elevated neopterin concentration is withdrawn from transfusion nationwide in Austria since 1994. With the introduction of additional neopterin screenings, the transfusion risk for an acute CMV, EBV or parvovirus B19-infection is significantly reduced. Some of the initially mainly at the Innsbruck blood donation center revealed data

have been confirmed by other researchers [9]. Investigations at the Technical University in Hong Kong show that also infections with SARS-virus or with Dengue virus can be detected sensitively [10, 11].

#### **Methods for neopterin measurements:**

Quantitative: ELISA (manually or fully automated), radioimmunoassay, high pressure liquid chromatography (HPLC), mostly for the determination of neopterin concentrations in urines with concomitant quantification of creatinine concentrations

Semi-quantitative: Rapid-test (at bed-side)

#### **Pre-analytics:**

Neopterin is sensitive to light. Therefore it is recommended to use dark tubes for collection of specimens or to wrap around an aluminum foil for

transportation. Serum and plasma specimens are of equal value. For measurement of neopterin concentrations in urine it is useful to apply first morning specimens and to relate neopterin to creatinine concentrations. At 4°C neopterin content in specimens remains stable for up to 3 days, in case when specimens are needed to be kept for longer periods, freezing is necessary (stability at -21°C: 3 months).

#### **Judgment of results:**

Upper limit of the normal (adults, 95<sup>th</sup> perc.):

Serum/plasma: 8.7 nmol/L

Cerebrospinal fluid: 5.5 nmol/L

Urine, slightly age-dependent (adults, 97.5<sup>th</sup> perc.):

Males: 176-229 µmol/mol creatinine; Females: 208-251 µmol/mol creatinine

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