

Contents

1 Pteridines	1
1.1 Historical remarks	2
1.2 Occurrence	2
1.3 Biosynthesis	3
1.4 Biochemical functions	4
1.4.1 Conjugated pteridines	4
1.4.2 Unconjugated pteridines	4
References	5
2 Neopterin	7
2.1 Chemical characteristics	7
2.2 Catabolism	8
2.3 Biochemical and physiological relevance	9
References	9
3 Measurement of Neopterin	13
3.1 Historical remarks	13
3.2 Measurement by reversed phase HPLC without pretreatment of samples	14
3.2.1 Principle	14
3.2.2 Collection of samples	14
3.2.3 Preparation of standard solutions	15
3.2.4 Procedure	15
3.2.5 Performance characteristics	17
3.3 Measurement of neopterin by reversed phase HPLC with on-line deproteinization	17
3.3.1 Principle	17
3.3.2 Apparatus	18
3.3.3 Collection of samples and preparation of standard solutions	19
3.3.4 Procedure	19
3.3.5 Performance characteristics	21
3.4 Measurement of neopterin by immunoassays	22
3.4.1 Principle	22
3.4.2 Procedure	22
3.4.3 Performance characteristics. Comparison with HPLC	23
References	23

4	Normal Ranges of Neopterin Concentrations in Various Body Fluids ..	25
4.1	Normal ranges of neopterin concentrations in urine	26
4.2	Normal ranges of neopterin concentrations in serum	28
4.3	Normal ranges of neopterin concentrations in cerebrospinal fluid ..	29
4.4	Normal ranges of neopterin concentrations in synovial fluid	30
4.5	Normal ranges of neopterin concentrations in saliva	31
4.6	Discussion	31
	References	31
5	Biosynthesis of Pteridines and the Human Immune System	33
5.1	Immunological activation and cytokines	33
5.2	Cytokines and pteridine biosynthesis	34
5.3	Inducers of pteridine synthesis in human cells	38
5.4	Cell culture techniques	40
5.4.1	Purification of human monocytes/macrophages from peripheral blood	40
5.4.2	Cultivation of peripheral blood mononuclear cells	44
5.4.3	Cultivation of cell lines	44
5.5	Determination of pteridines in cell homogenates and supernatants	44
5.5.1	Determination of neopterin in supernatants of macrophages or THP-1 cells to assess pteridine synthesis-activation potential of cytokines	45
5.5.2	Determination of intracellular levels of pteridines in cultured cells	45
5.6	Enzyme activities of pteridine synthesis in cell extracts	46
5.7	Biological significance of cytokine-induced pteridine synthesis	48
	References	52
6	Neopterin in Organ Transplantation	55
6.1	Renal transplantation	56
6.1.1	Neopterin concentrations in urine	56
6.1.2	Neopterin concentrations in serum and plasma	66
6.2	Transplantation of solid organs other than kidney	68
6.2.1	Neopterin in liver transplantation	69
6.2.2	Neopterin in heart transplantation	70
6.2.3	Neopterin in pancreas transplantation	72
6.3	Transplantation of bone marrow	72
6.3.1	Neopterin concentrations during the phase of bone marrow aplasia until engraftment	73
6.3.2	Neopterin concentrations and immunological complications after bone marrow transplantation	74
	References	74

7 Neopterin in Autoimmune Diseases and Related Inflammatory Disorders	77
7.1 Neopterin in rheumatoid arthritis	78
7.1.1 Neopterin concentrations in urine of patients with rheumatoid arthritis versus osteoarthritis	79
7.1.2 Neopterin concentrations in relation to stage and extent of rheumatoid arthritis	80
7.1.3 Neopterin concentrations in relation to clinical activity of rheumatoid arthritis	80
7.1.4 Neopterin and other laboratory variables for assessment of clinical activity in rheumatoid arthritis – linear discriminant analysis	82
7.1.5 Neopterin in urine and C-reactive protein for assessment of clinical activity in rheumatoid arthritis: generalized likelihood ratio model	84
7.1.6 Neopterin concentrations in other biological fluids from patients with rheumatoid arthritis	85
7.2 Neopterin in inflammatory bowel diseases	87
7.2.1 Neopterin and its value in assessment of clinical activity of <i>Crohn's</i> disease	88
7.2.2 Neopterin as marker of clinical activity in juvenile <i>Crohn's</i> disease	91
7.2.3 Neopterin as marker of clinical activity in patients with ulcerative colitis	92
7.2.4 Neopterin and cellular or soluble markers of T lymphocyte activation in patients with inflammatory bowel disease	93
7.3 Neopterin in autoimmune diabetes	95
7.4 Neopterin in autoimmune diseases of the thyroid	97
7.5 Neopterin in systemic lupus erythematosus	97
7.6 Neopterin in multiple sclerosis	99
7.7 Neopterin in sarcoidosis	101
7.8 Neopterin in celiac disease	104
References	105
8 Neopterin in Malignant Diseases	109
8.1 Hematological malignancies	110
8.1.1 Neopterin as an aid in diagnosis	110
8.1.2 Neopterin as a predictive marker	114
8.1.3 Neopterin and its correlation with interferon gamma and hemoglobin in hematological neoplasia	116
8.2 Gynecological malignancies	117
8.2.1 Neopterin in carcinoma of the uterine cervix	117
8.2.2 Neopterin in ovarian cancer	127
8.2.3 Neopterin in women with uterine sarcomas	140

8.3 Malignancies of the urogenital tract	144
8.3.1 Neopterin concentrations in various types of genitourinary tract malignancies	144
8.3.2 Neopterin and prognosis in prostatic carcinoma	146
8.4 Lung cancer	148
8.4.1 Neopterin concentrations in patients with various types of lung cancer	148
8.4.2 Neopterin and prognosis of lung cancer	151
8.5 Gastrointestinal, pancreatic and hepatic cancer	155
8.5.1 Neopterin concentrations in patients with various gastrointestinal and with pancreatic tumors	155
8.5.2 Neopterin values in gastrointestinal and pancreatic carcinomas after surgical therapy	158
8.5.3 Neopterin and prognosis of hepatocellular carcinoma	158
8.6 Breast cancer	161
8.7 Cancers of the head and neck region	163
8.8 Malignant melanoma	163
8.9 Neopterin in malignant diseases – a summary	164
References	165
9 Neopterin in Infectious Diseases	169
9.1 Infections by viruses	170
9.1.1 Neopterin concentrations in viral liver disease	170
9.1.2 Neopterin concentrations in other viral diseases	180
9.1.3 Neopterin and vaccination	184
9.2 Neopterin during infection by human immunodeficiency virus type 1 (HIV-1) and the acquired immunodeficiency syndrome (AIDS)	186
9.2.1 HIV-1 and the human immune system	187
9.2.2 Neopterin in HIV-1 infection – early results	188
9.2.3 Neopterin and the early phase of infection – an animal model	192
9.2.4 Neopterin concentrations in HIV-1 antibody negative and positive members of groups being at increased risk of contracting AIDS	195
9.2.5 Neopterin and its correlation with T cell subset data in HIV-1 related disease	201
9.2.6 Neopterin as a predictive marker for the course of HIV-1 disease	211
9.2.7 Neopterin and endogenous production of interferon gamma in patients infected with HIV-1	225
9.2.8 Neopterin in the central nervous system of patients with neurologic/psychiatric disorders related to HIV-1 disease	229

9.3 Infections by intracellular protozoa	237
9.3.1 Neopterin in malaria	237
9.3.2 Neopterin in human schistosomiasis mansonii	244
9.4 Infections by bacteria	247
9.4.1 Neopterin in lung tuberculosis	247
9.4.2 Neopterin in leprosy	248
9.4.3 Neopterin in melioidosis	249
9.4.4 Neopterin in Lyme neuroborreliosis	251
9.4.5 Neopterin and the differential diagnosis of bacterial and viral infections	252
9.5 Neopterin during sepsis and trauma	254
References	257
10 Monitoring of Immunostimulatory Therapy	265
References	272
11 Neopterin in Transfusion Medicine	275
References	280
Appendix	281
References	285
Subject Index	287