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ORIGINAL ARTICLE

Eosinopenia as a marker of diagnosis and prognostic to distinguish bacterial from aseptic meningitis in pediatrics

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Abstract

Procalcitonin (PCT) has proven its efficacy to distinguish bacterial from aseptic meningitis in children. Nevertheless, its use in routine is limited by its cost and availability, especially in low- and middle-income countries. It is now acknowledged that eosinopenia is a marker of infection and/or severity of the systemic inflammatory response. Although no study ever demonstrated that eosinopenia could differentiate bacterial from viral infection, we decided to conduct a study concerning meningitis in children. This bicentric and retrospective study was conducted between January 2012 and October 2018, in children hospitalized for meningitis. The white blood cell was systematically gathered at the admission to evaluate the eosinophil count. Characteristic data were compared between 2 groups: documented bacterial meningitis (DBP) and aseptic meningitis which includes documented viral meningitis (DVM) and non-documented meningitis (ND). Among 190 patients admitted for meningitis, 151 were analyzed, including DBM ($n = 45$), DVM ($n = 73$), and ND ($n = 33$) meningitis. Groups were comparable. Mean age was 33 ± 48 months with a sex ratio of 1.6. Mean of eosinophil count was 15 ± 34/mm^3 in the DBM group versus 132 ± 167/mm^3 for the aseptic meningitis group ($p < 0.0001$). Best threshold for the diagnosis of bacterial meningitis was an eosinophil count < 5/mm^3 with a sensitivity of 80% and specificity of 73% and a likelihood ratio of 2.9. Eosinopenia seems to be a reliable and non-invasive marker of bacterial meningitis in pediatrics. The absence of extra cost makes it very interesting in low- and middle-income countries or when usual biomarkers such as PCT are unavailable.

Keywords Eosinopenia · Meningitis · Bacterial · Viral · Biomarker

Introduction

Eosinopenia has been firstly described in 1893 by Zappert et al. in response to a systemic infection [1]. Thereafter in 1975, numerous studies confirmed that a decrease in eosinophil count was observed in case of acute inflammation, whereas we observe a normalization of the eosinophil count in case of healing [2–4]. Currently, this marker has been repurposed by specialists as an alternative to new and costly biomarkers.

Key points An eosinophil count < 100/mm^3 seems to be a relevant marker to diagnose a bacterial meningitis with a negative predictive value of 89%

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Up to day, there is no consensual definition of eosinopenia. Threshold may vary among different studies in the literature, with cutoff values from 10 to 140 eosinophil per cubic millimeter. Conversely, the normal value of eosinophil count ranges from 1 to 3% of the total leukocytes [5]. Therefore, we decided to choose a threshold of 1% namely below 100 eosinophils/mm^3 as the definition of eosinopenia in our work.

The physiopathology of eosinopenia during the acute infection is not well documented. It might be related to several factors involving chemokines responsible for a sequestration of eosinophils into the site of inflammation or a deflate of production of eosinophils from the bone marrow [3, 4, 6].

Eosinopenia has been already studied in the literature as a marker of infection, including in pediatrics. Indeed, a retrospective study with 34 hospitalized children suffering from infection (bacterial or viral) and 66 healthy volunteers showed that a decrease of eosinophil count was predictable of an acute infection (46 ± 58/mm^3 versus 288 ±

248/mm^3); meanwhile, the normalization of eosinophil count was associated with a favorable outcome (252 ± 162/mm^3) [7]. Another work recently published confirmed those observations in the diagnosis of early-onset neonatal sepsis [8] with a threshold of 140 eosinophils/mm^3. Authors found a relatively good specificity of this marker (90%) despite a moderate sensitivity (60%).

In an adult ward of internal medicine, an eosinophil count ≤ 10/mm^3 was considered of interest for the diagnosis of infection [9]. Recently, a new score called "CIBLE" (French translation of TARGET) has been proposed to guide the diagnosis of bacterial infection with a better sensitivity (72%) and a good specificity (77%) but requiring numerous medical information including past medical history [10].

To our knowledge, there is no study that evaluated the impact of eosinopenia to distinguish bacterial from viral infection. We decided to evaluate eosinopenia in case of meningitis, considering such condition is commonly documented by PCR and culture in the cerebrospinal fluid (CSF). The aim of our study is to evaluate whether the eosinophil count significantly differs between bacterial from viral meningitis in pediatrics.

Material and methods

We conducted a bicentric and retrospective study, from January 2012 to October 2018. We screened all the hospitalized children aged below 15 years and 3 months old, who presented a meningitis and where admitted in general pediatrics (Hôpital André Mignot, Le Chesnay, France) or in intensive care unit (ICU) (Hôpital Necker-Enfants malades, Paris, France). Diagnosis of meningitis was based on the presence of a clinical suspicion (meningeal syndrome) and confirmed by the lumbar puncture showing a pleiocytosis (> 5 leukocytes/mm^3) [11]. We excluded medical charts that were lacking eosinophil count in the white blood cell (WBC) count performed immediately at the emergency department before admission.

Thereafter, we divided our cohort into 3 groups depending on the analysis of the CSF: documented bacterial meningitis (DBM), documented viral meningitis (DVM), and non-documented meningitis (ND). In order to define a reproducible threshold of eosinopenia for the diagnostic of bacterial meningitis, we merged the DVM and ND into a group of aseptic meningitis. Secondary objective was to evaluate whether eosinopenia was associated with the severity of the infection, namely meningitis, and could be helpful to refer the patient to ICU.

Statistical analysis

Quantitative variables were expressed using mean and standard deviation. Qualitative variables were described by percentage. As the eosinophil count does not follow a normal distribution, comparisons were performed using non-parametric tests using the Kruskal-Wallis test for qualitative variables and the Wilcoxon test for binary variables. Statistical significance was defined for $p \leq 0.05$.

Results

Demographic data

During the study, 190 children were admitted for meningitis. Among them, 39 patients had no information on eosinophil count at admission due to the absence of a complete WBC count.

Overall, the flowchart was the following: 151 children were included and analyzed including 30% of DBM (n = 45), 48% of DVM (n = 73), and 22% of ND (n = 33) (Fig. 1).

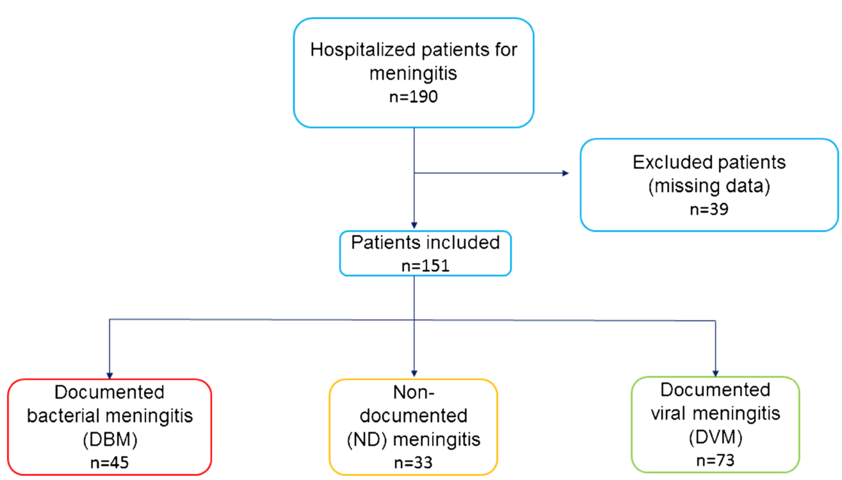

Fig. 1 Flowchart of the described population with meningitis

Table 1 Demographic characteristics of patients included

	Bacterial meningitis $n = 45$ (%)	Non-documented meningitis $n = 33$ (%)	Viral meningitis $w = 73$ (%)	p value
Sex				$p = 0.28$
Girls	19 (42)	8 (24)	31 (42)	
Boys	26 (58)	25 (76)	42 (58)	
Age				
Mean in month (SD)	31.7 (48.12)	64.28 (66.43)	19.78 (28.9)	$p = 0.0005$*
Prematurity	2 (4)	1 (3)	5 (7)	$p = 0.72$
Allergy	0	2 (6)	3 (4)	$p = 0.31$
Corticosteroid therapy	2 (4)	1 (3)	1 (1)	$p = 0.57$
Blood disorders	0 (0)	0 (0)	0 (0)	$p = 1$
Immunosuppression	2 (4)	2 (6)	1 (1)	$p = 0.38$

*No difference between bacterial meningitis and aseptic meningitis (including non-documented and viral meningitis) ($p = 0.82$)

Patient characteristics were comparable between groups (see Table 1). Sex ratio was of 1.6. Microorganisms involved in meningitis and methods used for their documentation are summarized in Table 2.

Impact of eosinophil count on the diagnosis of meningitis

Between groups of DBM, DVM, and ND meningitis, the mean of eosinophil count was statistically different ($p = 0.0001$) and confirmed between bacterial and aseptic meningitis (Fig. 2).

The usual markers performed for the diagnosis of bacterial meningitis, namely CRP, procalcitonin (PCT), proteinorachia, glycorachia, and lactatorachia, are reported in Table 3. For a threshold of eosinopenia defined $< 100/mm^3$, the area under the curve (AUC) was of 0.79 when dealing with absolute values of eosinophils and 0.80 in case of percentage. For comparison, AUC of CRP was better at 0.91 whereas PCT reached a value of 0.93 (Fig. 3).

For a lower threshold of eosinophil count $< 5/mm^3$, we obtained a high sensitivity (80%) with a 95% CI [65–90%] but a far better specificity (73%) with a 95% CI [63–81%] resulting in a likelihood ratio of 2.9.

Prognostic value of eosinophil count

Considering all individuals, 46% were hospitalized in general pediatrics whereas 54% required ICU. Interestingly, the eosinophil count was significantly lower for the children admitted in ICU ($p < 0.0001$) (Fig. 4).

Table 2 Microbiological features of meningitis

Meningitis	Microorganism		Diagnostic method	
Bacterial	*Streptococcus pneumoniae*	40%	CSF culture	60%
	Neisseria meningitidis	18%	CSF soluble antigen	31%
	Streptococcus agalactiae	16%	CSF direct examination	9%
	E. coli K1	7%	Blood culture	9%
	Listeria monocytogenes	4%	CSF PCR	7%
	Haemophilus influenzae b	4%	CSF serology	2%
	Staphylococcus aureus	2%	Skin biopsy	2%
	Enterococcus faecalis	2%		
	Borrelia burgdorferi	2%		
Viral	*Enterovirus*	85%	CSF PCR	100%
	Parechovirus	10%		
	Epstein-Barr virus	4%		
	Herpes simplex virus-1	1%		

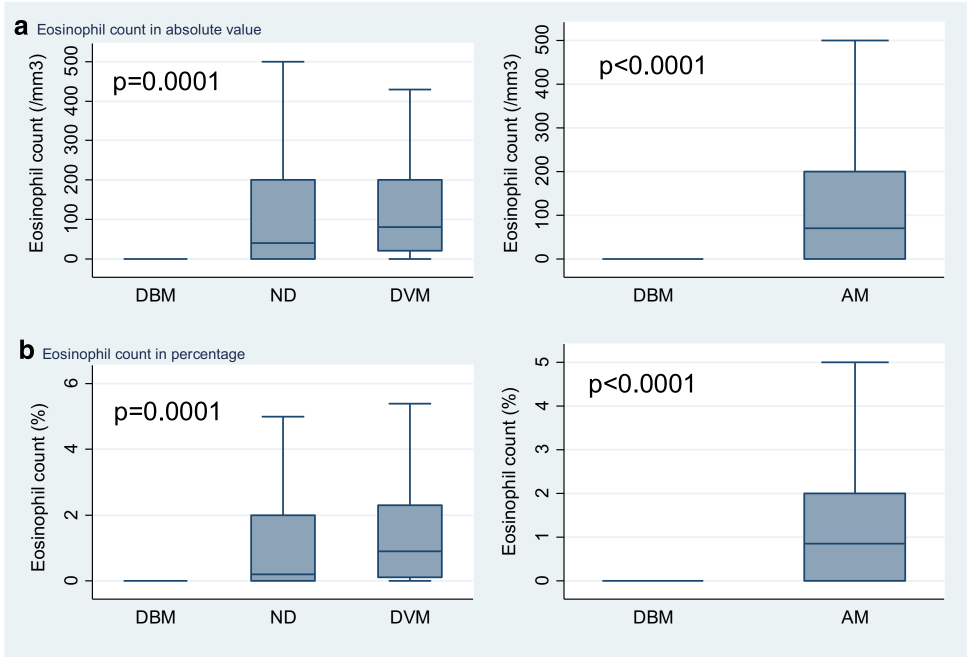

Fig. 2 Eosinophil count according to microbiological documentation. **a** Eosinophil count in absolute value. **b** Eosinophil count in percentage. DBM documented bacterial meningitis, ND non-documented, DVM documented viral meningitis

Also the duration of hospitalization (mean of 6 versus 3 days) and of antimicrobial therapy (mean of 3 versus 2 days) was significantly higher between eosinopenic children (< 100/ mm^3) than the ones without eosinopenia ($p < 0.001$ and $p = 0.01$, respectively).

Subgroup analyses

Further analyses have been performed to ensure that the findings were still relevant to distinguish bacterial from aseptic meningitis in children with general pediatrics and ICU. Results are summarized in Table 4.

Discussion

Our study seems to support that the deeper the eosinopenia is, the higher the specificity is to distinguish bacterial from aseptic meningitis in pediatrics. Indeed, an eosinophil count < 100/ mm^3 has a sensitivity of 87% and a specificity of 44% which can reach up to 73% if the eosinophil count is below 5/mm^3. Such marker is easily obtained with a simple blood sample without the need to wait for complementary biochemical tests which makes it helpful for a rapid orientation diagnosis of bacterial meningitis before the realization of a lumbar puncture. We believe that the presence of eosinopenia should guide the physician to determine whether the patient is deemed to require a rapid initiation of antimicrobial therapy, in addition to usual signs of orientation in case of meningitis. On one hand, the benefit of this particular marker is its early onset, in contrast with the microbiological cultures on CSF that require an average delay of 48 h [12]. On the other hand, numerous biomarkers are validated to differentiate bacterial from viral meningitis. For instance, several studies have demonstrated the usefulness of the PCT in children, including for the diagnosis of bacterial meningitis [13–15], with a very high sensitivity (99%) and specificity (83%) for a threshold of 0.5 ng/mL [14]. Yet in our study, only 64% of the cases with

Table 3 Comparison of meningitis biomarkers

	Eosinopenia	CRP	PCT	CSF protein	CSF glucose	CSF lactate
Threshold	100/mm^3	5 mg/L	0.5 ng/mL	0.5 g/L	2/3 blood glucose (mmol/L)	3.2 mmol/L
Se (%)	87	100	91	88	93	67
Sp (%)	44	40	86	53	22	83
PPV (%)	40	40	67	43	28	44
NPV (%)	89	100	97	92	91	93

Se sensibility, *Sp* specificity, *PPV* positive predictive value, *NPV* negative predictive value

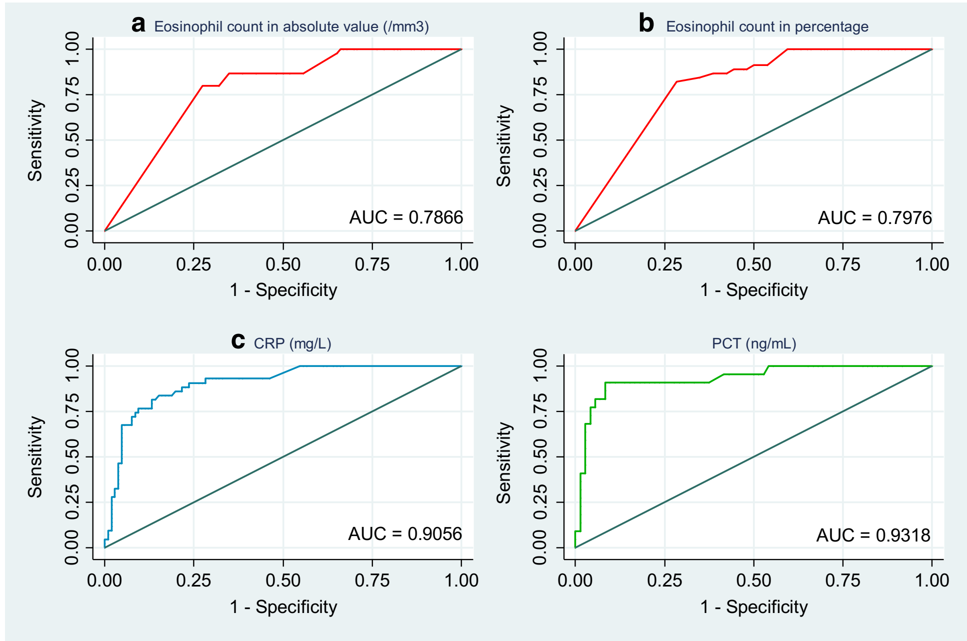

Fig. 3 ROC curves comparing CRP, PCT, and eosinophil count as a diagnostic tool. **a** Eosinophil count in absolute value (/mm^3). **b** Eosinophil count in percentage

a DBM had an elevated PCT. Moreover, false positive are possible [16] and its elevated cost limits its use in routine. Likewise, CRP is known to be elevated in case of infection, but failed to distinguish clearly bacterial from viral meningitis [17]. Other common markers such as PMN in the CSF [18], glycorachia, proteinorachia, or lactatorachia [19–21] require the realization of a lumbar puncture and thus cannot be directly compared to eosinopenia. Moreover, hypoglycorachia and hyperproteinorachia commonly a good sign of bacterial meningitis in adults are often missing in children [22] and can be encountered in case of viral meningitis [18].

Furthermore, scores have been developed but most of them also require some items from the CSF. In 1989, Spanos et al. proposed a complicated calculation hardly applicable in clinical practice [23]. In addition in 1995, Hoen et al. suggested the use of a new and simpler score, with a very high negative predictive value (NPV) of 99% for the diagnosis of bacterial meningitis in adults and children [24]. Later on in 2002,

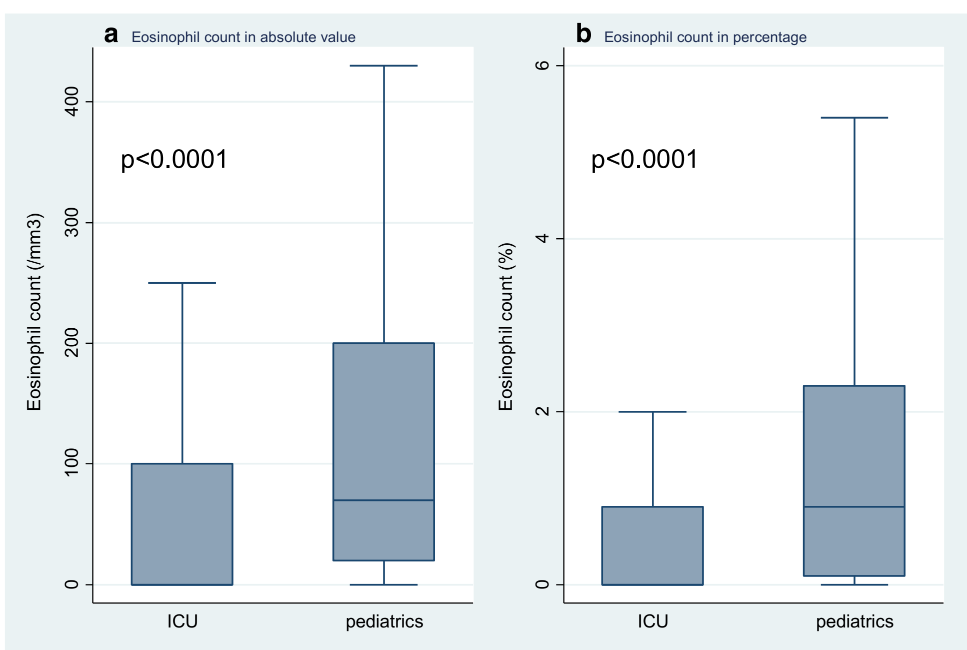

Fig. 4 Eosinophil count according to hospitalization ward. **a** Eosinophil count in absolute value. **b** Eosinophil count in percentage. ICU intensive care unit

Table 4 Subgroup analyses: comparison of meningitis in general pediatrics versus ICU

Hospitalization ward	Meningitis	Eosinophil count in absolute value (/mm^3) (mean ± standard deviation)	*p* value	Eosinophil count in percentage (%) (mean ± standard deviation)	*p* value
ICU	Bacterial ($n = 41$)	14 ± 33	0.0004	0.11 ± 0.30	0.0005
	Aseptic ($n = 40$)	119 ± 175		1.13 ± 1.66	
General pediatrics	Bacterial ($n = 4$)	28 ± 55	0.05	0.20 ± 0.40	0.026
	Aseptic ($n = 66$)	140 ± 163		2.30 ± 6.81	

Nigrovic et al. published the Bacterial Meningitis Score (BMS) which is only validated in children and can exclude the diagnosis of bacterial meningitis with about 100% of NPV [25–27]. Also, Chavanet et al. proposed in 2007 the Meningitest, a repurposed BMS with a 100% NPV but positive predictive value of only 54% [28].

Interestingly, a number of studies compared eosinopenia to CRP and PCT for the diagnosis of sepsis [29, 30] or bacteremia [31] and concluded that eosinopenia was not the best biomarker.

Other studies intend to show the interest of eosinophil count for the diagnostic of infection without success [32–34]. However, its prognostic value at admission in pediatric ICU [32] and in adults [35, 36] to predict mortality. In our work, eosinopenia also revealed to be a relevant prognostic biomarker and was significantly associated with the severity and the orientation between ICU and general pediatrics in the limit of our small sample size.

Our study has several limitations. First, it is a retrospective study with a limited sample size ($n = 151$). Second, we could not evaluate if the normalization of the eosinophil count operated after an effective antimicrobial therapy for the DBP, as previously described [37] which would have supported our findings. Third, it would have been insightful to conduct such a study in low- and middle-income countries, where helminthes are endemic and responsible of hypereosinophilia. Indeed, our results might not be extrapolated to such countries, where the cost-effectiveness of our marker is crucial. In the same way, we did not exclude on purpose allergic patients, the ones with a hematological disorder, immunodepression, or under corticosteroids, considering that those data are often lacking at the emergency department. However, it has been shown that eosinophil count of allergic children has the same kinetic over time than healthy individuals [38].

In conclusion, the presence of eosinopenia at the admission of children presenting meningitis is a simple diagnostic and prognostic tool to differentiate quickly bacterial from aseptic meningitis. Although its sensitivity remains lower than the PCT, eosinopenia has not competitor when such biomarkers are unavailable or doable in routine. We believe its cost-effectiveness makes it particularly attractive in low- and middle-income countries. A larger study is necessary to confirm those findings that are only applicable to meningitis and pediatrics.

Contributors' statement Dr. D and Miss D conceptualized and designed the study, carried out the initial analyses, coordinated and supervised data collection, drafted the initial manuscript, and reviewed and revised the manuscript.

Professor S, Drs. M and N designed the data collection instruments, collected data, and reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval/informed consent was not required, as part as a routine care in a retrospective observational study.

Conflict of interest The authors declare that they have no conflict of interest.

Abbreviations PCT, procalcitonin; DBP, documented bacterial meningitis; DVM, documented viral meningitis; ND, non-documented meningitis

References

1. Zappert J (1893) Ueber das Vorkommen der Eosinophilen Zellen in menschlichen Blute. Z Klin Med 23:227–308
2. Bass DA, Gonwa TA, Szejda P, Cousart MS, DeChatelet LR, McCall CE (1980) Eosinopenia of acute infection: production of eosinopenia by chemotactic factors of acute inflammation. J Clin Invest 65(6):1265–1271
3. Bass DA (1975) Behavior of eosinophil leukocytes in acute inflammation. I. Lack of dependence on adrenal function. J Clin Invest 55(6):1229
4. Bass DA (1975) Behavior of eosinophil leukocytes in acute inflammation. II. Eosinophil dynamics during acute inflammation. J Clin Invest 56(4):870–879
5. Rothenberg ME (1998) Eosinophilia. N Engl J Med 338(22):1592–1600
6. Hogan SP, Rosenberg HF, Moqbel R et al (2008) Eosinophils: biological properties and role in health and disease. Clin Exp Allergy 38(5):709–750

7. Montesanti M, Testa G, Biagi C, Bartolini F (1997) Trend of circulating eosinophils in healthy children and children suffering from infectious diseases. A retrospective study. Minerva Pediatr 49(5): 179–186
8. Wilar R (2018) Diagnostic value of eosinopenia and neutrophil to lymphocyte ratio on early onset neonatal sepsis. Korean J Pediatr
9. Karakonstantis S, Gryllou N, Papazoglou G, Lydakis C (2018) Eosinophil count (EC) as a diagnostic and prognostic marker for infection in the internal medicine department setting. Rom J Intern Med. https://doi.org/10.2478/rjim-2018-0039
10. Bouldoires B, Gil H, Soumagne T, Humbert S, Meaux Ruault N, Magy Bertrand N (2018) A predictive bacterial infection score according to eosinophil level: an observational study. Rev Med Interne 39(1):10–16
11. SPILF. 17ème conférence de consensus en thérapeutique anti-infectieuse : Prise en charge des méningites bactériennes aiguës communautaires (à l'exclusion du nouveau-né), texte de recommandations. Paris; 2008. [Internet]. Disponible sur: http://www.infectiologie.com/UserFiles/File/medias/_documents/consensus/Meningites_consensus-long.pdf. Accessed Apr 2018
12. Bryant K, Marshall GS (1999) Most cerebrospinal fluid cultures in children with bacterial meningitis are positive within two days. Pediatr Infect Dis J 18(8):732–733
13. Gendrel D, Raymond J, Assicot M et al (1998) Procalcitonin, C-reactive protein and interleukin 6 in bacterial and viral meningitis in children. Presse Medicale Paris Fr 1983. 27(23):1135–1139
14. Dubos F, Korczowski B, Aygun DA et al (2008) Serum procalcitonin level and other biological markers to distinguish between bacterial and aseptic meningitis in children: a European multicenter case cohort study. Arch Pediatr Adolesc Med 162(12): 1157–1163
15. Prat C, Domínguez J, Rodrigo C et al (2004) Use of quantitative and semiquantitative procalcitonin measurements to identify children with sepsis and meningitis. Eur J Clin Microbiol Infect Dis 23(2):136–138
16. Sanaei Dashti A, Alizadeh S, Karimi A, Khalifeh M, Shoja SA (2017) Diagnostic value of lactate, procalcitonin, ferritin, serum-C-reactive protein, and other biomarkers in bacterial and viral meningitis: a cross-sectional study. Medicine (Baltimore) 96(35):e7637
17. Hansson LO, Axelsson G, Linné T, Aurelius E, Lindquist L (1993) Serum C-reactive protein in the differential diagnosis of acute meningitis. Scand J Infect Dis 25(5):625–630
18. Negrini B, Kelleher KJ, Wald ER (2000) Cerebrospinal fluid findings in aseptic versus bacterial meningitis. Pediatrics 105(2):316–319
19. Komorowski RA, Farmer SG, Knox KK (1986) Comparison of cerebrospinal fluid C-reactive protein and lactate for diagnosis of meningitis. J Clin Microbiol 24(6):982
20. Viallon A, Desseigne N, Marjollet O et al (2011) Meningitis in adult patients with a negative direct cerebrospinal fluid examination: value of cytochemical markers for differential diagnosis. Crit Care 15(3):R136
21. Kleine TO, Zwerenz P, Zöfel P, Shiratori K (2003) New and old diagnostic markers of meningitis in cerebrospinal fluid (CSF). Brain Res Bull 61(3):287–297
22. Bonadio WA (1992) The cerebrospinal fluid: physiologic aspects and alterations associated with bacterial meningitis. Pediatr Infect Dis J 11(6):423–431
23. Spanos A, Harrell FE, Durack DT (1989) Differential diagnosis of acute meningitis: an analysis of the predictive value of initial observations. JAMA. 262(19):2700–2707
24. Hoen B, Viel JF, Paquot C, Gérard A, Canton P (1995) Multivariate approach to differential diagnosis of acute meningitis. Eur J Clin Microbiol Infect Dis 14(4):267–274
25. Nigrovic LE, Kuppermann N, Malley R (2002) Development and validation of a multivariable predictive model to distinguish bacterial from aseptic meningitis in children in the post-Haemophilus influenzae era. Pediatrics. 110(4):712–719
26. Nigrovic LE, Kuppermann N, Macias CG et al (2007) Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. JAMA 297(1):52–60
27. Piérart J, Lepage P (2006) Value of the « Bacterial Meningitis Score » (BMS) for the differential diagnosis of bacterial versus viral meningitis. Rev Med Liege 61(7–8):581–585
28. Chavanet P, Schaller C, Levy C et al (2007) Performance of a predictive rule to distinguish bacterial and viral meningitis. J Inf Secur 54(4):328–336
29. Shaaban H, Daniel S, Sison R, Slim J, Perez G (2010) Eosinopenia: is it a good marker of sepsis in comparison to procalcitonin and C-reactive protein levels for patients admitted to a critical care unit in an urban hospital? J Crit Care 25(4):570–575
30. Garnacho-Montero J, Huici-Moreno MJ, Gutiérrez-Pizarraya A et al (2014) Prognostic and diagnostic value of eosinopenia, C-reactive protein, procalcitonin, and circulating cell-free DNA in critically ill patients admitted with suspicion of sepsis. Crit Care 18(3):R116
31. Ho KM, Towler SC (2009) A comparison of eosinopenia and C-reactive protein as a marker of bloodstream infections in critically ill patients: a case control study. Anaesth Intensive Care 37(3):450–456
32. Kim YH, Park HB, Kim MJ et al (2013) Prognostic usefulness of eosinopenia in the pediatric intensive care unit. J Korean Med Sci 28(1):114–119
33. Wibrow BA, Ho KM, Flexman JP, Keil AD, Kohrs DL (2011) Eosinopenia as a diagnostic marker of bloodstream infection in hospitalised paediatric and adult patients: a case-control study. Anaesth Intensive Care 39(2):224–230
34. Setterberg MJ, Newman W, Potti A, Smego RA (2004) Utility of eosinophil count as predictor of bacteremia. Clin Infect Dis 38(3): 460–461
35. Abidi K, Belayachi J, Derras Y et al (2011) Eosinopenia, an early marker of increased mortality in critically ill medical patients. Intensive Care Med 37(7):1136–1142
36. Merino CA, Martínez FT, Cardemil F, Rodríguez JR (2012) Absolute eosinophils count as a marker of mortality in patients with severe sepsis and septic shock in an intensive care unit. J Crit Care 27(4):394–399
37. Davido B, Makhloufi S, Matt M et al (2017) Changes in eosinophil count during bacterial infection: revisiting an old marker to assess the efficacy of antimicrobial therapy. Int J Infect Dis 61:62–66
38. Montesanti M, Testa G, Biagi C, Bartolini F (1997) Pattern of circulating eosinophils in allergic children suffering from infectious disease. Minerva Pediatr 49(5):187–191