

Secondary hemophagocytic lymphohistiocytosis in zoonoses. A systematic review

A. CASCIO¹⁻³, L.M. PERNICE¹, G. BARBERI¹, D. DELFINO¹, C. BIONDO⁴, C. BENINATI⁴, G. MANCUSO⁴, A.J. RODRIGUEZ-MORALES^{3,5}, C. IARIA^{2,6}

¹Department of Human Pathology, Policlinico "G. Martino", Messina, Italy

²AILMI (Associazione Italiana per la Lotta contro le Malattie Infettive) (Italian Association for the Control of Infectious Diseases), University of Messina, Messina, Italy

³Working Group on Zoonoses, International Society for Chemotherapy

⁴Elie Metchnikoff Department, University of Messina, Messina, Italy

⁵Universidad Tecnológica de Pereira and Especialización en Epidemiología, Fundación Universitaria del Área Andina, Pereira, Colombia

⁶Infectious Diseases Unit, Azienda Ospedaliera Piemonte-Papardo, Messina, Italy

Abstract. - BACKGROUND: Hemophagocytic lymphohistiocytosis (HLH) is a rare syndrome that is often fatal despite treatment. It is caused by a dysregulation in natural killer T-cell function, resulting in activation and proliferation of histiocytes with uncontrolled hemophagocytosis and cytokines overproduction. The syndrome is characterized by fever, hepatosplenomegaly, cytopenias, liver dysfunction, and hyperferritinemia. HLH can be either primary, with a genetic aetiology, or secondary, associated with malignancies, autoimmune diseases, or infections.

AIM: To focus on secondary HLH complicating zoonotic diseases.

MATERIALS AND METHODS: PubMed search of human cases of HLH occurring during zoonotic diseases was performed combining the terms (haemophagocytic OR haemophagocytosis OR hemophagocytosis OR hemophagocytic OR erythrophagocytosis OR macrophage activation syndrome) with each one of the etiological agents of zoonoses.

RESULTS: Among bacterial diseases, most papers reported cases occurring during brucellosis, rickettsial diseases and Q fever. Regarding viral diseases, most of the cases were reported in patients with avian influenza A subtype H5N1. Among the protozoan zoonoses, most of the cases were reported in patients with visceral leishmaniasis. Regarding zoonotic fungi, most of the cases were reported in AIDS patient with histoplasmosis. No cases of secondary HLH were reported in patient with zoonotic helminthes.

CONCLUSIONS: Zoonotic diseases are an important cause of HLH. Secondary HLH can delay the correct diagnosis of the zoonotic disease, and can contribute to an adverse outcome.

Key Words:

Hemophagocytic lymphohistiocytosis (HLH), Zoonoses, Developing Countries, Epidemiology, Review.

Introduction

Although zoonotic infections are a major burden worldwide – both in terms of immediate and long-term morbidity and mortality^{1,2} and in terms of socioeconomical, ecological, and political impact³ – scientific and public health interest and funding for these diseases remain relatively minor and inadequate⁴. In the present review we will focus on secondary hemophagocytic lymphohistiocytosis (HLH) complicating zoonotic diseases.

HLH is a potentially fatal hyperinflammatory syndrome that is characterized by histiocyte proliferation and hemophagocytosis. HLH may be inherited (primary, familial) and occurs generally in infants or may be secondary to infection, malignancy or rheumatologic conditions, thereby, occurring at any age. The former is a syndrome associated with autosomal recessive disorders that lead to defects in apoptosis induction of virus-infected cells or tumor cells by cytolytic immune cells, including natural killer (NK) cells or cytotoxic T lymphocytes (CTL). Defects of cytotoxic activities of NK or CTL cells, X-linked lymphoproliferative syndrome type 1 (XLP1) and type 2 (XLP2) can also lead to HLH development⁵. Secondary HLH, called also macrophage activation syndrome (MAS), is a common finding in systemic juvenile idiopathic arthritis (sJIA) in which, an apparent

hybrid situation is present. In fact, several mutations have been reported recently in sJIA⁶. Thus, as in other infection-associated hyperinflammatory syndromes⁷⁻¹⁰, activation of receptors and cells of the innate immunity system is likely to play a major role in HLH.

The most typical presenting signs and symptoms are fever, hepatosplenomegaly, and cytopenias. Less frequently observed clinical findings are neurological symptoms, lymphadenopathy, edema, skin rash, and jaundice^{11,12}. Common laboratory findings include hypertriglyceridemia, hyperferritinemia, a coagulopathy with hypofibrinogenemia, and elevated aminotransferases^{11,12}. However, HLH is diagnosed using clinical criteria developed by the HLH Study Group of the Histiocyte Society^{13,14} (Table I).

Literature Review

PubMed search of human cases of HLH occurring during zoonotic diseases was performed

combining the terms (haemophagocytic, or haemophagocytosis, or hemophagocytosis, or hemophagocytic, or erythrophagocytosis, or macrophage activation syndrome) with each one of the etiological agents of zoonoses and/or one of the diseases indicated in Tables II and III for the period January 1950 to August 2012. A study was considered eligible for inclusion in the systematic review if it reported data on patients with zoonotic diseases who had microscopic signs of hemophagocytosis and/or fulfilled the diagnostic criteria of the HLH Study Group of the Histiocyte Society.

Results

The PubMed search identified 1157 papers. Duplicate publications or papers not reporting clinical cases were excluded. After a scrupulous analysis, 153 papers were further evaluated. In the Table

Table I. HLH 2004 Diagnostic criteria (modified from ref.^{13,14}).

<p>The diagnosis of HLH can be established if one of either 1 or 2 below is fulfilled:</p> <ol style="list-style-type: none"> 1. A molecular diagnosis consistent with HLH 2. Diagnostic criteria for HLH are fulfilled (five out of the eight criteria below):
<ul style="list-style-type: none"> • Fever • Splenomegaly • Cytopenias (affecting ≥ 2 lineages in the peripheral blood): <ul style="list-style-type: none"> Hemoglobin < 90 g/l (in infants < 4 weeks: hemoglobin < 100 g/l) Platelets $< 100.000/ml$ Neutrophils $< 1000/ml$ • Hypertriglyceridemia and/or hypofibrinogenemia: <ul style="list-style-type: none"> Fasting triglycerides ≥ 265 mg/dl Fibrinogen ≤ 1.5 g/L • Hemophagocytosis in bone marrow or spleen or lymphnodes • Low or absent NK-cell activity • Ferritin ≥ 500 $\mu g/l$ • Soluble CD25 ≥ 2400 U/L
<p>Comments:</p> <ol style="list-style-type: none"> (1) If hemophagocytic activity is not proven at the time of presentation, further search for hemophagocytic activity is encouraged. If the bone marrow specimen is not conclusive, material may be obtained from other organs. Serial marrow aspirates over time may also be helpful. (2) The following findings may provide strong supportive evidence for the diagnosis: (a) spinal fluid pleocytosis (mononuclear cells) and/or elevated spinal fluid protein, (b) histological picture in the liver resembling chronic persistent hepatitis (biopsy). (1) Other abnormal clinical and laboratory findings consistent with the diagnosis are: cerebromeningeal symptoms, lymph node enlargement, jaundice, edema, skin rash. Hepatic enzyme abnormalities, hypoproteinemia, hyponatremia, VLDL \uparrow, HDL \downarrow.

Table II. Clinical significant agents of zoonoses found associated with secondary HLH.

Bacteria	References and notes
<i>Anaplasma phagocytophilum</i>	¹⁵ Review
Bartonella sp.	¹⁶ Renal transplant recipients
<i>Borrelia</i> sp.	¹⁷ Lyme disease
<i>Brucella</i> sp.	¹⁸ Analysis of children with brucellosis associated with pancytopenia, Turkey; ¹⁹ 8 year-old male, Turkey; ²⁰ 84 year-old female, antilymphoma chemotherapy; ²¹ Multicenter retrospective study, Turkey; ²² Retrospective study, 3 patients, Turkey; ²³ 11 year-old boy, Turkey; ²⁴ 5 patients, Spain; ^{25,26} disseminated intravascular coagulation, Spain; ^{27,28} ; Retrospective study, Saudi Arabia; ^{29,30} Two and half years old female, India; ³¹ Pulmonary involvement, Iran; ³² Bone marrow biopsy findings in brucellosis patients with hematologic abnormalities, China;
<i>Campylobacter</i> sp.	³³ <i>Campylobacter fetus</i> , AIDS, USA
<i>Capnocytophaga</i> sp	³⁴ Sudden Sensorineural Hearing Loss, Japan
<i>Clostridium</i> sp.	³⁵ AIDS; ³⁶ Pancreatic carcinoma
<i>Coxiella burnetii</i>	^{37,38,39,37,38,40}
<i>Ehrlichia chaffeensis</i> and <i>Ehrlichia ewingii</i>	⁴¹ Two children, USA; ⁴² Case report, USA; ⁴³ Fatal case, USA; ⁴⁴ 67 year-old white man, disseminated intravascular coagulopathy, USA
<i>Leptospira</i> sp.	India ^{45,46} Fatal case, Taiwan:
<i>Listeria</i> sp.	⁴⁷ <i>L. monocytogenes</i> , bone marrow transplant recipient, France
<i>Mycobacterium avium</i>	⁴⁸ <i>M. avium</i> , AIDS; ⁴⁹ <i>M. avium</i> , Lupus erythematosus
<i>Orientia tsutsugamushi</i>	50-53
<i>Rickettsia</i> spp	⁵⁴ Murine typhus in returned travelers; ⁵⁵ MSF, Italy; ^{52,56} <i>Rickettsia conorii</i> ; ⁵⁷ MSF; ⁵⁸ MSF, Israel; ⁵⁹ Fulminant Rocky Mountain spotted fever
<i>Salmonella</i> sp. (excluding <i>S. typhi</i>)	⁶⁰ Child suffering from chronic granulomatous disease, associated with septicemia due to <i>Salmonella typhi</i> murium; ⁶¹
Viruses	
Crimean-Congo haemorrhagic fever virus	⁶²⁻⁶⁸ Turkey
Hantaviruses	⁶⁹ Hemorrhagic fever with renal syndrome, South Korea. ⁷⁰ Hemorrhagic fever with renal syndrome
Hepatitis E virus	⁷¹ Japan.
Influenza viruses	⁷²⁻⁷⁷ influenza A virus H5N1 subtype; ⁷⁸ Fatal case of swine influenza virus in an immunocompetent host, USA
SARS coronavirus	⁷⁹⁻⁸² China, Taiwan
Protozoa	
<i>Babesia</i> sp.	⁸³⁻⁸⁵ Splenectomized renal allograft recipient, USA
<i>Leishmania</i> spp.	⁸⁶ Children with HLH treated at the University Children's Hospital in Belgrade; ⁸⁷⁻⁸⁹ Chronic granulomatous disease; ⁹⁰ Four childhood cases; China; ⁹¹ immunocompetent adult-case report and review; ⁹² A review of situation in Thailand; ⁹³ Retrospective study Clinical analysis on 28 patients with hemophagocytic lymphohistiocytosis syndrome, China; ⁹⁴ Two cases, India; ⁹⁵ AIDS, India; ⁹⁶ 28 years man, India; ⁹⁷ 9 cases, India; ⁹⁸ Illustrative case and review, India; ⁹⁹ Fatal case, India; ¹⁰⁰ Retrospective study, India; ¹⁰¹ Cerebrospinal fluid involvement, Oman; ¹⁰² Nine cases, Saudi Arabia. ¹⁰³ 4,5 month-old infant associated with H1N1 virus infection, Turkey; ¹⁰⁴ Adolescent, Turkey; ¹⁰⁵ Child, Turkey; ¹⁰⁶ Child; Turkey; ¹⁰⁷ 4 year-old boy travel history, Turkey; ¹⁰⁸ 5 year-old boy, Turkey; ¹⁰⁹ 18 Turkish children (2 weeks-72 months); ¹¹⁰ Child, pseudomonas septicemia, myelodysplasia, Turkey ¹¹¹ Greece; ¹¹² Epstein Barr, Cyprus; ¹¹³ 2 year-old child, Israel; ¹¹⁴ 46 year-old woman, Israel;

Table continue

Table II. (Continued). Clinical significant agents of zoonoses found associated with secondary HLH.

Bacteria	References and notes
Protozoa	
<i>Leishmania</i> spp.	¹¹⁵ 20 month-old boy, Tunisia; ¹¹⁶ 2 year-old boy, Tunisia; ¹¹⁷ Tunisia; ¹¹⁸ 2 severe cases, Tunisia; ¹¹⁹ 15 month-old girl, Travel Spain, Norway; ¹²⁰ 7 year-old previously healthy Czech boy, travel in Italy; ¹²¹ 16 month-old girl, Spain; ¹²² Spain; ¹²³ Spain; ¹²⁴ Spain; ¹²⁵ Pericardial effusion, Spain; ¹²⁶ Rheumatoid arthritis, adalimumab, Spain; ¹²⁷ steroid, bronchial asthma, Spain; ¹²⁸ France; ¹²⁹ France; ¹³⁰ 12 month-old girl, France; ¹³¹ 12 cases, France
<i>Toxoplasma gondii</i>	^{132,133} Primary disseminated toxoplasmosis; ^{134,16,135} renal transplantation; ¹³⁶ Bone marrow transplantation; ^{137,138,139} AIDS
Fungi	
<i>Cryptococcus neoformans</i>	¹⁴⁰ A child case, cryptococcal meningoencephalitis, Japan
<i>Histoplasma capsulatum</i>	^{139, 141-149} AIDS; ¹⁵⁰ AIDS Reconstitution inflammatory syndrome; ¹⁵¹ Pediatric AIDS
<i>Penicillium marneffei</i>	^{152,153} Leukemia; ¹⁵⁴ 21-year-old man with Still's disease; ^{155,156} Adult-onset Still's disease, adalimumab, ¹⁵⁷ Kidney transplant recipients, USA; ¹⁵⁸ Heart transplant recipient, USA; ¹⁵⁹ 6 year-old boy with chronic mucocutaneous candidiasis, USA; ¹⁶⁰ Sarcoidosis on chronic steroid treatment, USA; ¹⁶¹ France; ¹⁶² Immunocompetent, India; ¹⁶³ 2 cases, India; ¹⁶⁴ Fungal endocarditis, chronic hepatitis C, cryoglobulinemia, renal failure and <i>Staphylococcus aureus</i> perinephric abscess and bacteremia
	¹⁶⁵ AIDS, China; ¹⁶⁶ AIDS, Thailand; ¹⁶⁷ Thailand; ¹⁶⁸ China

Table III. Bacterial, viral, fungal and helminthic agents of zoonoses not associated with secondary HLH.

Bacteria	<i>Bacillus antraci</i> , <i>Chlamydothyla psittaci</i> , <i>Corynebacterium ulcerans</i> , <i>Escherichia coli</i> O157H7, <i>Francisella tularensis</i> , <i>Helicobacter</i> sp, <i>Mycobacterium bovis</i> , <i>Mycobacterium caprae</i> , <i>Mycobacterium marinum</i> , <i>Mycobacterium microti</i> , <i>Mycobacterium ulcerans</i> , <i>Mycobacterium genavense</i> , <i>Mycobacterium malmoense</i> , and <i>Mycobacterium farcinogenes</i> , <i>Pasteurella</i> sp. <i>Shigella</i> sp., <i>Staphylococcus aureus</i> (clearly associated to animal reservoir), <i>Streptococcus suis</i> , <i>Streptococcus equi</i> , <i>Streptococcus canis</i> , <i>Streptococcus acidominimus</i> , <i>Streptococcus bovis</i> , <i>Vibrio</i> sp. (excluding <i>Vibrio cholera</i>), <i>Yersinia</i> sp.
Viruses	Borna disease virus, California serogroup viruses, Chikungunya virus, Cowpox virus, Ebola virus, Hendra virus, Japanese encephalitis virus, Kyasanur forest disease virus, Lassa virus, Lymphocytic choriomeningitis virus, Marburg virus, Monkeypox virus, Nipah virus, Omsk haemorrhagic fever virus, Oropouche virus, Rabies and lyssaviruses, Rift Valley fever virus, Ross River virus, Sindbis virus, Tick-borne encephalitis, Venezuelan equine encephalitis virus, West Nile virus, Yellow fever virus, Zika virus
Protozoa	<i>Balantidium coli</i> , <i>Blastocystis hominis</i> , <i>Cryptosporidium parvum</i> , <i>Giardia lamblia</i> , <i>Plasmodium knowlesi</i> , <i>Trypanosoma brucei</i> , <i>Trypanosoma cruzi</i>
Fungi	<i>Basidiobolus rana rum</i> , <i>Malassezia</i> spp., <i>Microsporium</i> spp., <i>Paracoccidioides brasiliensis</i> , <i>Trichophyton</i> spp.
Helminths	<i>Ancylostoma</i> spp., <i>Angiostrongylus</i> spp., <i>Clonorchis sinensis</i> and <i>Opisthorchis</i> spp., <i>Diphyllobothrium</i> spp, <i>Dirofilaria</i> spp., <i>Echinococcus</i> spp., <i>Echinococcus</i> spp., <i>Fasciola</i> spp., <i>Fasciolopsis buski</i> , <i>Gnathostoma</i> spp., <i>Paragonimus</i> spp., <i>Thelazia</i> spp., <i>Toxocara</i> spp., <i>Trichinella</i> spp.

II are reported all the agents of zoonoses associated with secondary HLH, while in the second column of Table III are listed zoonotic agents not associated with secondary HLH.

Among bacterial diseases, 15 papers reported cases occurring during brucellosis, 16 during rickettsial diseases (*Rickettsia* spp, *Orientia* sp, *Ehrlichia* spp and *Anaplasma* spp), 6 during Q

fever, 2 during leptospirosis. One paper each reported papers during Lyme disease or *Capnocytophaga* sp. infection. Most of the above papers described cases of secondary HLH occurring in immunocompetent patients without important comorbidities. Cases of *Bartonella*, *Clostridium*, *Listeria*, *Mycobacterium*, *Salmonella* spp and *Campylobacter fetus* infections were less reported and most of them occurred in patients with major comorbidities. Among the zoonotic mycobacterial diseases, HLH was reported only in patients with *Mycobacterium avium* infection affected by HIV infection or by systemic lupus erythematosus.

Among viral diseases, cases were reported in patients with avian influenza A subtype H5N1, swine influenza, SARS coronavirus, Crimean–Congo haemorrhagic fever, hepatitis E virus. Most of cases occurred in immunocompetent patients without important comorbidities.

Regarding the protozoan zoonoses, most of the cases were reported in patients with visceral leishmaniasis. Only in few cases of the 46 articles reporting such cases, comorbidities were present. Nine papers reported cases occurring in patients with toxoplasmosis and most of them were immunocompromised. Two cases were reported in patient with babesiosis.

Regarding zoonotic fungi, 23, four and one paper reported cases occurring in patients with *Histoplasma capsulatum*, *Penicillium marneffei* and *Cryptococcus neoformans* infections, respectively. Most of them occurred in immunocompromised patients. No cases of secondary HLH were reported in patient with zoonotic helminths.

In one case each, a double infection with Epstein Barr virus¹¹², H1N1 virus¹⁰³, *Pseudomonas* septicemia,¹¹⁰ and *Staphylococcus aureus* perinephric abscess¹⁶⁴, in addition to the zoonotic agent, were reported.

Regarding comorbidities, five papers reported cases occurring in kidney transplant recipients^{16,134,135,157}, one in a heart transplant recipient¹⁵⁸ and two in bone marrow transplant recipients^{47,136}. Twenty papers reported cases occurring in HIV-infected patients^{33,48,95,137-139,141-151,165,166}, of them, one occurred in a pediatric patient¹⁶⁵, and one in the course of AIDS Reconstitution Inflammatory Syndrome¹⁵⁰. In two and four papers leukaemia^{152,153} and chronic granulomatous disease (CGD)^{60,87-89}, respectively, were present. Other major comorbidities reported were rheumatologic diseases^{49,126,154-156}, which in three cases were under treatment with adalimumab^{126,155,156}.

Other major comorbidities/immunosuppressive conditions were chronic steroid treatment^{127,160}, chronic mucocutaneous candidiasis¹⁵⁹, antilymphoma chemotherapy²⁰, and pancreatic carcinoma³⁶. Five papers reported cases occurring after travel to endemic zones^{54,80,107,119,169}.

Discussion

Zoonotic infections are defined, in general, as infections transmitted from animal to man (and less frequently vice versa), either directly (through direct contact or contact with animal products) or indirectly (through an intermediate vector as an arthropod or an insect)¹⁷⁰. The main zoonotic features of influenza are represented by the role of animal hosts as reservoirs and substrates for the development of novel strains, and their role in the introduction of these strains into human pathology. Avian H5N1 influenza is a typical zoonotic infection, requiring close contact with infected animal hosts¹. The current H1N1 pandemic strain stopped being zoonotic after human-to-human transmission emerged as the cause of the pandemic. The single non-human hosts for each of influenza B and influenza C viruses play a minimal role in human disease¹. Avian influenza A subtype H5N1 infection and severe acute respiratory syndrome (SARS) due to coronavirus (SARS-CoV) share similar pathologic features. Pneumocytes are the primary target of infection, resulting in diffuse alveolar damage. Systemic cytokine activation results in hemophagocytic syndrome, lymphoid depletion, and skeletal muscle fiber necrosis¹⁷¹. However, HLH has also been found in fatal cases of H1N1 infection during the pandemic which emerged in April 2009¹⁷².

HIV infection alone or in the presence of other opportunistic and non-opportunistic infections or malignancies has been associated with HLH, and HLH has also been described in the setting of immune reconstitution inflammatory syndrome^{150,173,174}.

Also rotavirus infection can cause secondary HLH¹⁷⁵, but this is not a frequent finding¹⁷⁶⁻¹⁸⁰. Of note, animal rotaviruses might be able to cross species barriers, and lack of systematic surveillance of rotavirus infection in small animals hinders the ability to establish firm epidemiological connections^{178,180-182}.

Almost all the cases associated with bacterial infections were due intracellular organisms frequently causing epatosplenomegaly and leukope-

nia such as *Brucella* and *Rickettsia* spp. Early treatment of brucellosis with appropriate antibiotics will be life-saving¹⁸³⁻¹⁸⁷. We believe that HLH should always be considered in the severe cases of rickettsial diseases, especially if associated with pancytopenia^{186,188-194}. More studies are needed to understand whether immunosuppressive treatments (e.g. with steroids) could be beneficial (as we suspect), especially in those cases not responding promptly to antibiotic therapy⁵⁵. No cases were reported in the course of *Escherichia coli* O157H7 infection, even though in a cirrhosis patient a case caused by *E. coli* infection secondary to bacterial translocation has been described¹⁹⁵⁻¹⁹⁷.

Leishmania donovani and *Leishmania infantum* can cause HLH. Moreover *Leishmania* infection by itself can mimic the syndrome, especially in the presence of organomegaly and cytopenia¹⁹⁸⁻²⁰⁵. A bone marrow aspirate determines the correct diagnosis²⁰⁶⁻²⁰⁹. Treatment of leishmaniasis-associated haemophagocytic syndrome with amphotericin B results in cure^{108,210-214}.

Pulmonary involvement in HLH has been reported in some severe cases³¹. Occurrence of pulmonary involvement is quite frequent especially in HLH triggered by viral infections^{72-78,183,215-220}.

Being rare itself, HLH is diagnosed almost exclusively in seriously ill, hospitalized patients. Diagnosis of secondary HLH may be laborious, but the primary source must be continually sought, particularly in the case of rare pathogens. Furthermore, it should be stressed that the identification of hemophagocytosis in bone marrow aspirate represents only one of 5-8 criteria needed for the diagnosis of HLH²²¹. Treatment of secondary HLH is dependent on its cause. Infectious agents should be eradicated promptly, along with administering supportive care. There are no randomized trials for primary HLH, due to the rarity of this disease. Treatment is based on the combination of immune suppression (such as cyclosporin A) and chemotherapy (such as etoposide)^{222,223}. Intravenous immunoglobulins may also be beneficial¹¹⁴. Treatment should be started without delay, yet it should be kept in mind that the use of immunosuppression may further delay diagnosis and definitive treatment.

Conclusions

Zoonotic diseases are an important cause of HLH. Secondary HLH can delay the correct di-

agnosis of the zoonotic disease, and can contribute to an adverse outcome. Further studies are needed to understand whether an immunosuppressive treatment could be beneficial in those cases that do not promptly respond to anti-infective therapy.

References

- 1) CHRISTOU L. The global burden of bacterial and viral zoonotic infections. *Clin Microbiol Infect* 2011; 17: 326-330.
- 2) AKRITIDIS N. Parasitic, fungal and prion zoonoses: an expanding universe of candidates for human disease. *Clin Microbiol Infect* 2011; 17: 331-335.
- 3) CASCIO A, BOSILKOVSKI M, RODRIGUEZ-MORALES AJ, PAPPAS G. The socio-ecology of zoonotic infections. *Clin Microbiol Infect* 2011; 17: 336-342.
- 4) PAPPAS G, CASCIO A, RODRIGUEZ-MORALES AJ. The immunology of zoonotic infections. *Clin Dev Immunol* 2012; 2012: 208508.
- 5) TANG YM, XU XJ. Advances in hemophagocytic lymphohistiocytosis: pathogenesis, early diagnosis/differential diagnosis, and treatment. *SciWorld J* 2011; 11: 697-708.
- 6) STEPHAN JL, KONE-PAUT I, GALAMBRUN C, MOUY R, BADER-MEUNIER B, PRIEUR AM. Reactive haemophagocytic syndrome in children with inflammatory disorders. A retrospective study of 24 patients. *Rheumatology (Oxford)* 2001; 40: 1285-1292.
- 7) BIONDO C, MALARA A, COSTA A, SIGNORINO G, CARDILE F, MIDIRI A, GALBO R, PAPERGI S, DOMINA M, PUGLIESE M, TETI G, MANCUSO G, BENINATI C. Recognition of fungal RNA by TLR7 has a nonredundant role in host defense against experimental candidiasis. *Eur J Immunol* 2012; doi: 10.1002/eji.201242532.
- 8) CARDACI A, PAPERGI S, MIDIRI A, MANCUSO G, DOMINA M, CARICCIO VL, MANDANICI F, GALBO R, LO PASSO C, PERNICE I, DONATO P, RICCI S, BIONDO C, TETI G, FELICI F, BENINATI C. Protective activity of *Streptococcus pneumoniae* Spr1875 protein fragments identified using a phage displayed genomic library. *PLoS One* 2012; 7: e36588.
- 9) COSTA A, GUPTA R, SIGNORINO G, MALARA A, CARDILE F, BIONDO C, MIDIRI A, GALBO R, TRIEU-CUOT P, PAPERGI S, TETI G, HENNEKE P, MANCUSO G, GOLENBOCK DT, BENINATI C. Activation of the NLRP3 inflammasome by group B streptococci. *J Immunol* 2011; 188: 1953-1960.
- 10) BIONDO C, SIGNORINO G, COSTA A, MIDIRI A, GERACE E, GALBO R, BELLANTONI A, MALARA A, BENINATI C, TETI G, MANCUSO G. Recognition of yeast nucleic acids triggers a host-protective type I interferon response. *Eur J Immunol* 2011; 41: 1969-1979.
- 11) ARICO M, JANKA G, FISCHER A, HENTER JI, BLANCHE S, ELINDER G, MARTINETTI M, RUSCA MP. Hemophagocytic lymphohistiocytosis. Report of 122 children

- from the International Registry. FHL Study Group of the Histiocyte Society. *Leukemia* 1996; 10: 197-203.
- 12) JANKA GE. Familial hemophagocytic lymphohistiocytosis. *Eur J Pediatr* 1983; 140: 221-230.
 - 13) GUPTA S, WEITZMAN S. Primary and secondary hemophagocytic lymphohistiocytosis: clinical features, pathogenesis and therapy. *Expert Rev Clin Immunol* 2010; 6: 137-154.
 - 14) HENTER JI, HORNE A, ARICO M, EGELER RM, FILIPOVICH AH, IMASHUKU S, LADISCH S, MCCLAIN K, WEBB D, WINIARSKI J, JANKA G. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2007; 48: 124-131.
 - 15) DUMLER JS. The biological basis of severe outcomes in *Anaplasma phagocytophilum* infection. *FEMS Immunol Med Microbiol* 2012; 64: 13-20.
 - 16) KARRAS A, THERVET E, LEGENDRE C. Hemophagocytic syndrome in renal transplant recipients: report of 17 cases and review of literature. *Transplantation* 2004; 77: 238-243.
 - 17) CANTERO-HINOJOSA J, DIEZ-RUIZ A, SANTOS-PEREZ JL, AGUILAR-MARTINEZ JL, RAMOS-JIMENEZ A. Lyme disease associated with hemophagocytic syndrome. *Clin Invest* 1993; 71: 620.
 - 18) AKBAYRAM S, DOGAN M, AKGUN C, PEKER E, PARLAK M, CAKSEN H, ONER AF. An analysis of children with brucellosis associated with pancytopenia. *Pediatr Hematol Oncol* 2011; 28: 203-208.
 - 19) ERDURAN E, MAKULOGLU M, MUTLU M. A rare hematological manifestation of brucellosis: reactive hemophagocytic syndrome. *J Microbiol Immunol Infect* 2010; 43: 159-162.
 - 20) MENESES A, EPAULARD O, MAURIN M, GRESSIN R, PAVESE P, BRION JP, GARIN-BASTUJI B, STAHL JP. [Brucella bacteremia reactivation 70years after the primary infection.]. *Med Mal Infect* 2009.
 - 21) Sari I, Altuntas F, Hacıoğlu S, Kocyigit I, Sevinc A, Sacar S, Deniz K, Alp E, Eser B, Yildiz O, Kaynar L, Unal A, Cetin M. A multicenter retrospective study defining the clinical and hematological manifestations of brucellosis and pancytopenia in a large series: Hematological malignancies, the unusual cause of pancytopenia in patients with brucellosis. *Am J Hematol* 2008; 83: 334-339.
 - 22) KARAKUKCU M, PATIROGLU T, OZDEMIR MA, GUNES T, GUMUS H, KARAKUKCU C. Pancytopenia, a rare hematologic manifestation of brucellosis in children. *J Pediatr Hematol Oncol* 2004; 26: 803-806.
 - 23) YILDIRMAK Y, PALANDUZ A, TELHAN L, ARAPOGLU M, KAYAALP N. Bone marrow hypoplasia during *Brucella* infection. *J Pediatr Hematol Oncol* 2003; 25: 63-64.
 - 24) MARTIN-MORENO S, SOTO-GUZMAN O, BERNALDO-DE-QUIROS J, REVERTE-CEJUDO D, BASCONES-CASAS C. Pancytopenia due to hemophagocytosis in patients with brucellosis: a report of four cases. *J Infect Dis* 1983; 147: 445-449.
 - 25) ZUAZU JP, DURAN JW, JULIA AF. Hemophagocytosis in acute brucellosis. *N Engl J Med* 1979; 301: 1185-1186.
 - 26) LOPEZ-GOMEZ M, HERNANDEZ J, SAMPALO A, BIEDMA A, ALCALA A, MATEAS F. Reactive hemophagocytic syndrome with disseminated intravascular coagulation secondary to acute brucellosis. *Enferm Infecc Microbiol Clin* 1994; 12: 519-520.
 - 27) ULLRICH CH, FADER R, FAHNER JB, BARBOUR SD. Brucellosis presenting as prolonged fever and hemophagocytosis. *Am J Dis Child* 1993; 147: 1037-1038.
 - 28) AL-EISSA Y, AL-NASSER M. Haematological manifestations of childhood brucellosis. *Infection* 1993; 21: 23-26.
 - 29) ANDREO JA, VIDAL JB, HERNANDEZ JE, SERRANO P, LOPEZ VM, SORIANO J. Hemophagocytic syndrome associated with brucellosis. *Med Clin (Barc)* 1988; 90: 502-505.
 - 30) MONDAL N, SURESH R, ACHARYA NS, PRAHARAJ I, HARISH BN, MAHADEVAN S. Hemophagocytic syndrome in a child with brucellosis. *Indian J Pediatr* 2010; 77: 1434-1436.
 - 31) HEYDARI AA, AHMADI F, SARVGHAD MR, SAFARI H, BAJOURI A, SAEIDPOUR M. Hemophagocytosis and pulmonary involvement in brucellosis. *Int J Infect Dis* 2007; 11: 89-90.
 - 32) DEMIR C, KARAHOCAGIL MK, ESEN R, ATMACA M, GONULLU H, AKDENIZ H. Bone marrow biopsy findings in brucellosis patients with hematologic abnormalities. *Chin Med J (Engl)* 2012; 125: 1871-1876.
 - 33) ANSTEAD G, JORGENSEN J, CRAIG F, BLASER M, PATTERSON T. Thermophilic multidrug-resistant *Campylobacter fetus* infection with hypersplenism and histiocytic phagocytosis in a patient with acquired immunodeficiency syndrome. *Clin Infect Dis* 2001; 32: 295-296.
 - 34) TAMURA A, MATSUNOBU T, KURITA A, SHIOTANI A. Hemophagocytic syndrome in the course of sudden sensorineural hearing loss. *ORL J Otorhinolaryngol Relat Spec* 2012; 74: 211-214.
 - 35) RAMON I, LIBERT M, GUILLAUME MP, CORAZZA F, KARMALI R. Recurrent haemophagocytic syndrome in an HIV-infected patient. *Acta Clin Belg* 2010; 65: 276-278.
 - 36) CHINEN K, OHKURA Y, MATSUBARA O, TSUCHIYA E. Hemophagocytic syndrome associated with clostridial infection in a pancreatic carcinoma patient. *Pathol Res Pract* 2004; 200: 241-245.
 - 37) ESTROV Z, BRUCK R, SHTALRID M, BERREBI A, RESNITZKY P. Histiocytic hemophagocytosis in Q fever. *Arch Pathol Lab Med* 1984; 108: 7.
 - 38) HUFNAGEL M, NIEMEYER C, ZIMMERHACKL LB, TUCHELMANN T, SAUTER S, BRANDIS M. Hemophagocytosis: a complication of acute Q fever in a child. *Clin Infect Dis* 1995; 21: 1029-1031.
 - 39) CHEN TC, CHANG K, LU PL, LIU YC, CHEN YH, HSIEH HC, YANG WC, LIN WR, TSAI JJ, LIN SF. Acute Q fever with hemophagocytic syndrome: case report and literature review. *Scand J Infect Dis* 2006; 38: 1119-1122.
 - 40) HARRIS P, DIXIT R, NORTON R. *Coxiella burnetii* causing haemophagocytic syndrome: a rare complication of an unusual pathogen. *Infection* 2011; 39: 579-582.

- 41) HANSON D, WALTER AW, POWELL J. Ehrlichia-induced hemophagocytic lymphohistiocytosis in two children. *Pediatr Blood Cancer* 2010; 56: 661-663.
- 42) BURNS S, SAYLORS R, MIAN A. Hemophagocytic lymphohistiocytosis secondary to Ehrlichia chaffeensis infection: a case report. *J Pediatr Hematol Oncol* 2010; 32: e142-143.
- 43) MARTY AM, DUMLER JS, IMES G, BRUSMAN HP, SMRKOVSKI LL, FRISMAN DM. Ehrlichiosis mimicking thrombotic thrombocytopenic purpura. Case report and pathological correlation. *Hum Pathol* 1995; 26: 920-925.
- 44) ABBOTT KC, VUKELJA SJ, SMITH CE, McALLISTER CK, KONKOL KA, O'ROURKE TJ, HOLLAND CJ, RISTIC M. Hemophagocytic syndrome: a cause of pancytopenia in human ehrlichiosis. *Am J Hematol* 1991; 38: 230-234.
- 45) KRISHNAMURTHY S, MAHADEVAN S, MANDAL J, BASU D. Leptospirosis in association with hemophagocytic syndrome: a rare presentation. *Indian J Pediatr* 2012. DOI: 10.1007/s12098-012-0863-0
- 46) YANG CW, PAN MJ, WU MS, CHEN YM, TSEN YT, LIN CL, WU CH, HUANG CC. Leptospirosis: an ignored cause of acute renal failure in Taiwan. *Am J Kidney Dis* 1997; 30: 840-845.
- 47) LAMBOTTE O, FIIHMAN V, POYART C, BUZYN A, BERCHE P, SOUMELIS V. Listeria monocytogenes skin infection with cerebritis and haemophagocytosis syndrome in a bone marrow transplant recipient. *J Infect* 2005; 50: 356-358.
- 48) PELLEGRIN JL, MERLIO JP, LACOSTE D, BARBEAU P, BROSSARD G, BEYLOT J, LENG B. Syndrome of macrophagic activation with hemophagocytosis in human immunodeficiency virus infection. *Rev Med Interne* 1992; 13: 438-440.
- 49) YANG WK, FU LS, LAN JL, SHEN GH, CHOU G, TSENG CF, CHI CS. Mycobacterium avium complex-associated hemophagocytic syndrome in systemic lupus erythematosus patient: report of one case. *Lupus* 2003; 12: 312-316.
- 50) KWON HJ, YOO IH, LEE JW, CHUNG NG, CHO B, KIM HK, KANG JH. Life-threatening Scrub Typhus with Hemophagocytosis and Acute Respiratory Distress Syndrome in an Infant. *J Trop Pediatr* 2012. doi: 10.1093/tropej/fms030
- 51) VALSALAN R, KOSARAJU K, SOHANLAL T, KUMAR PS. Hemophagocytosis in scrub typhus. *J Postgrad Med* 2010; 56: 301-302.
- 52) PREMARATNA R, WILLIAMS HS, CHANDRASENA TG, RAJAPAKSE RP, KULARATNA SA, DE SILVA HJ. Unusual pancytopenia secondary to haemophagocytosis syndrome in rickettsioses. *Trans R Soc Trop Med Hyg* 2009; 103: 961-963.
- 53) JAYAKRISHNAN MP, VENY J, FEROZE M. Rickettsial infection with hemophagocytosis. *Trop Doct* 2011; 41: 111-112.
- 54) WALTER G, BOTELHO-NEVERS E, SOCOLOVSKI C, RAOULT D, PAROLA P. Murine typhus in returned travelers: a report of thirty-two cases. *Am J Trop Med Hyg* 2012; 86: 1049-1053.
- 55) CASCIO A, GIORDANO S, DONES P, VENEZIA S, IARIA C, ZIINO O. Haemophagocytic syndrome and rickettsial diseases. *J Med Microbiol* 2011; 60: 537-542.
- 56) PEREZ-DE PEDRO I, MACIAS-VEGA N, MIRANDA-CANDON I, CAMPS-GARCIA MT. [Severe Rickettsia conorii infection associated with hemophagocytic syndrome]. *Enferm Infecc Microbiol Clin* 2008; 26: 597-598.
- 57) SOTTO A, CORNE P, BESSIS D, LAMAURY I, TAIB J, JANBON F. Hemophagocytosis syndrome in Mediterranean boutonneuse fever. *Presse Med* 1994; 23: 1582.
- 58) BERNER Y, KEYSARY A, BERREBI A. Transient histiocytic hemophagocytosis and pancytopenia in Mediterranean spotted fever. *Isr J Med Sci* 1989; 25: 660-661.
- 59) KODURI PR. Fulminant Rocky Mountain spotted fever: a hemophagocytic syndrome? *Crit Care Med* 1996; 24: 365-366.
- 60) BENZ-LEMOINE E, BORDIGONI P, SCHAACK JC, BRIQUEL E, CHICLET AM, OLIVE D. Systemic reactive histiocytosis with hemophagocytosis and hemostasis disorders associated with septic granulomatosis. *Arch Fr Pediatr* 1983; 40: 179-182.
- 61) GUTIERREZ-RAVE PECERO V, LUQUE MARQUEZ R, AYERZA LERCHUNDI M, CANAVATE ILLESCAS M, PRADOS MADRONA D. Reactive hemophagocytic syndrome: analysis of a series of 7 cases. *Med Clin (Barc)* 1990; 94: 130-134.
- 62) DILBER E, CAKIR M, ERDURAN E, KOKSAL I, BAHAT E, MUTLU M, CELTIK AY, OKTEN A. High-dose methylprednisolone in children with Crimean-Congo haemorrhagic fever. *Trop Doct* 2010; 40: 27-30.
- 63) ERDURAN E, CAKIR M. Reactive hemophagocytic lymphohistiocytosis and Crimean-Congo hemorrhagic fever. *Int J Infect Dis* 2010; 14 Suppl 3: e349; author reply e350.
- 64) BARUT S, DINCER F, SAHIN I, OZYURT H, AKKUS M, ERKORKMAZ U. Increased serum ferritin levels in patients with Crimean-Congo hemorrhagic fever: can it be a new severity criterion? *Int J Infect Dis* 2009; 14: e50-54.
- 65) DILBER E, CAKIR M, ACAR EA, ORHAN F, YARIS N, BAHAT E, OKTEN A, ERDURAN E. Crimean-Congo hemorrhagic fever among children in north-eastern Turkey. *Ann Trop Paediatr* 2009; 29: 23-28.
- 66) CAGATAY A, KAPMAZ M, KARADENIZ A, BASARAN S, YENEREL M, YAVUZ S, MIDILLI K, OZSUT H, ERAKSOY H, CALANGU S. Haemophagocytosis in a patient with Crimean Congo haemorrhagic fever. *J Med Microbiol* 2007; 56: 1126-1128.
- 67) TASDELEN FISGIN N, FISGIN T, TANYEL E, DOGANCI L, TULEK N, GULER N, DURU F. Crimean-Congo hemorrhagic fever: five patients with hemophagocytic syndrome. *Am J Hematol* 2008; 83: 73-76.
- 68) KARTI SS, ODABASI Z, KORTEN V, YILMAZ M, SONMEZ M, CAYLAN R, AKDOGAN E, EREN N, KOKSAL I, OVALI E, ERICKSON BR, VINCENT MJ, NICHOL ST, COMER JA, ROLLIN PE, KSIAZEK TG. Crimean-Congo hemorrhagic fever in Turkey. *Emerg Infect Dis* 2004; 10: 1379-1384.
- 69) LEE JJ, CHUNG IJ, SHIN DH, CHO SH, CHO D, RYANG DW, KHAN AS, KIM HJ. Hemorrhagic fever with renal

- syndrome presenting with hemophagocytic lymphohistiocytosis. *Emerg Infect Dis* 2002; 8: 209-210.
- 70) BATY V, SCHUHMACHER H, BOURGOIN C, LATGER V, BUISINE J, MAY T, CANTON P. Hemophagocytic syndrome and hemorrhagic fever with renal syndrome. *Presse Med* 1998; 27: 1577.
 - 71) KAMIHIRA T, YANO K, TAMADA Y, MATSUMOTO T, MIYAZATO M, NAGAOKA S, OHATA K, ABIRU S, KOMORI A, DAIKOKU M, YATSUHASHI H, ISHIBASHI H. Case of domestically infected hepatitis E with marked thrombocytopenia. *Nihon Shokakibyō Gakkai Zasshi* 2008; 105: 841-846.
 - 72) ZHANG Z, ZHANG J, HUANG K, LI KS, YUEN KY, GUAN Y, CHEN H, NG WF. Systemic infection of avian influenza A virus H5N1 subtype in humans. *Hum Pathol* 2009; 40: 735-739.
 - 73) LU M, XIE ZG, GAO ZC, WANG C, LI N, LI M, SHAO HQ, WANG YP, GAO ZF. Histopathologic study of avian influenza H5N1 infection in humans. *Zhonghua Bing Li Xue Za Zhi* 2008; 37: 145-149.
 - 74) ZHANG W, WEN LY, LU M, XIONG Y, QIAN KJ, DENG AH, GUO LS, XIAO ZK, ZHAO XS, DUAN SM, XIE ZG, GAO ZF, LI M, SHAO HQ, WANG GG, LIU DW, GAO ZC. Clinical characteristic analysis of the first human case infected by influenza A (H5N1) in Jiangxi Province. *Zhonghua Jie He He Hu Xi Za Zhi* 2006; 29: 300-306.
 - 75) HENTER JI, CHOW CB, LEUNG CW, LAU YL. Cytotoxic therapy for severe avian influenza A (H5N1) infection. *Lancet* 2006; 367: 870-873.
 - 76) CHAN PK. Outbreak of avian influenza A(H5N1) virus infection in Hong Kong in 1997. *Clin Infect Dis* 2002; 34 Suppl 2: S58-64.
 - 77) TO KF, CHAN PK, CHAN KF, LEE WK, LAM WY, WONG KF, TANG NL, TSANG DN, SUNG RY, BUCKLEY TA, TAM JS, CHENG AF. Pathology of fatal human infection associated with avian influenza A H5N1 virus. *J Med Virol* 2001; 63: 242-246.
 - 78) KIMURA K, ADLAKHA A, SIMON PM. Fatal case of swine influenza virus in an immunocompetent host. *Mayo Clin Proc* 1998; 73: 243-245.
 - 79) NICHOLLS JM, POON LL, LEE KC, NG WF, LAI ST, LEUNG CY, CHU CM, HUI PK, MAK KL, LIM W, YAN KW, CHAN KH, TSANG NC, GUAN Y, YUEN KY, PEIRIS JS. Lung pathology of fatal severe acute respiratory syndrome. *Lancet* 2003; 361: 1773-1778.
 - 80) HSUEH PR, CHEN PJ, HSIAO CH, YEH SH, CHENG WC, WANG JL, CHIANG BL, CHANG SC, CHANG FY, WONG WW, KAO CL, YANG PC. Patient data, early SARS epidemic, Taiwan. *Emerg Infect Dis* 2004; 10: 489-493.
 - 81) ZAJKOWSKA JM, HERMANOWSKA-SZPAKOWICZ T, PANCEWICZ S, KONDRUSIK M, GRYGORCZUK S. Severe acute respiratory syndrome (SARS)--new, unknown disease?. *Pol Merkur Lekarski* 2004; 16: 183-187.
 - 82) PEI F, ZHENG J, GAO ZF, ZHONG YF, FANG WG, GONG EC, ZOU WZ, WANG SL, GAO DX, XIE ZG, LU M, SHI XY, LIU CR, YANG JP, WANG YP, HAN ZH, SHI XH, DAO WB, GU J. Lung pathology and pathogenesis of severe acute respiratory syndrome: a report of six full autopsies. *Zhonghua Bing Li Xue Za Zhi* 2005; 34: 656-660.
 - 83) AUERBACH M, HAUBENSTOCK A, SOLOMAN G. Systemic babesiosis. Another cause of the hemophagocytic syndrome. *Am J Med* 1986; 80: 301-303.
 - 84) SLOVUT DP, BENEDETTI E, MATAS AJ. Babesiosis and hemophagocytic syndrome in an asplenic renal transplant recipient. *Transplantation* 1996; 62: 537-539.
 - 85) GUPTA P, HURLEY RW, HELSETH PH, GOODMAN JL, HAMMERSCHMIDT DE. Pancytopenia due to hemophagocytic syndrome as the presenting manifestation of babesiosis. *Am J Hematol* 1995; 50: 60-62.
 - 86) KRIVOKAPIC-DOKMANOVIC L, KRSTOVSKI N, JANKOVIC S, LAZIC J, RADLOVIC N, JANIC D. Clinical characteristics and disease course in children with haemophagocytic lymphohistiocytosis treated at the University Children's Hospital in Belgrade. *Srp Arh Celok Lek* 2012; 140: 191-197.
 - 87) ALVAREZ-CARDONA A, RODRIGUEZ-LOZANO AL, BLANCA-GALICIA L, RIVAS-LARRAURI FE, YAMAZAKI-NAKASHIMADA MA. Intravenous immunoglobulin treatment for macrophage activation syndrome complicating chronic granulomatous disease. *J Clin Immunol* 2012; 32: 207-211.
 - 88) MARTIN A, MARQUES L, SOLER-PALACIN P, CARAGOL I, HERNANDEZ M, FIGUERAS C, ESPANOL T. Visceral leishmaniasis associated hemophagocytic syndrome in patients with chronic granulomatous disease. *Pediatr Infect Dis J* 2009; 28: 753-754.
 - 89) SOLER-PALACIN P, MARGARETO C, LLOBET P, ASENSIO O, HERNANDEZ M, CARAGOL I, ESPANOL T. Chronic granulomatous disease in pediatric patients: 25 years of experience. *Allergol Immunopathol (Madr)* 2007; 35: 83-89.
 - 90) GUO X, CHEN N, WANG TY, ZHOU CY, LI Q, GAO J. Visceral leishmaniasis associated hemophagocytic lymphohistiocytosis: report of four childhood cases. *Zhonghua Er Ke Za Zhi* 2011; 49: 550-553.
 - 91) KOUBAA M, MAALLOUL I, MARRAKCHI C, MDHAFFAR M, LAHIANI D, HAMMAMI B, MAKNI F, AYEDI A, JEMAA MB. Hemophagocytic syndrome associated with visceral leishmaniasis in an immunocompetent adult-case report and review of the literature. *Ann Hematol* 2012; 91: 1143-1145.
 - 92) WIWANITKIT V. Bone marrow leishmaniasis: a review of situation in Thailand. *Asian Pac J Trop Med* 2011; 4: 757-759.
 - 93) SHU MM, ZHU HF, ZHANG T, GAO GX, CHEN XQ. Clinical analysis on 28 patients with hemophagocytic lymphohistiocytosis syndrome. *Zhongguo Shi Yan Xue Ye Xue Za Zhi* 2010; 18: 463-465.
 - 94) PRASAD R, MUTHUSAMI S, PANDEY N, TILAK V, SHUKLA J, MISHRA OP. Unusual presentations of Visceral leishmaniasis. *Indian J Pediatr* 2009; 76: 843-845.
 - 95) PATEL KK, PATEL AK, SARDA P, SHAH BA, RANJAN R. Immune reconstitution visceral leishmaniasis presented as hemophagocytic syndrome in a patient with AIDS from a nonendemic area: a case report. *J Int Assoc Physicians AIDS Care (Chic)* 2009; 8: 217-220.

- 96) BHUTANI V, DUTTA U, DAS R, SINGH K. Hemophagocytic syndrome as the presenting manifestation of visceral leishmaniasis. *J Assoc Physicians India* 2002; 50: 838-839.
- 97) PAHWA R, SINGH T, KHURANA N. Hemophagocytic syndrome in malaria and kala-azar. *Indian J Pathol Microbiol* 2004; 47: 348-350.
- 98) RAJAGOPALA S, DUTTA U, CHANDRA KS, BHATIA P, VARMA N, KOCHHAR R. Visceral leishmaniasis associated hemophagocytic lymphohistiocytosis--case report and systematic review. *J Infect* 2008; 56: 381-388.
- 99) MATHUR P, SAMANTARAY JC, SAMANTA P. Fatal haemophagocytic syndrome and hepatitis associated with visceral leishmaniasis. *Indian J Med Microbiol* 2007; 25: 416-418.
- 100) BHATIA P, HALDAR D, VARMA N, MARWAHA R, VARMA S. A case series highlighting the relative frequencies of the common, uncommon and atypical/unusual hematological findings on bone marrow examination in cases of visceral leishmaniasis. *Mediterr J Hematol Infect Dis* 2011; 3: e2011035.
- 101) FATHALLA M, HASHIM J, ALKINDY H, WALI Y. Cerebrospinal fluid involvement in a case of visceral leishmaniasis associated with hemophagocytic lymphohistiocytosis. *Sultan Qaboos Univ Med J* 2007; 7: 253-256.
- 102) AL-SOHAIBANI MO. Bone marrow histopathological changes in visceral leishmaniasis. *Ann Saudi Med* 1996; 16: 304-307.
- 103) AY Y, YILDIZ B, UNVER H, KARAPINAR DY, VARDAR F. Hemophagocytic lymphohistiocytosis associated with H1N1 virus infection and visceral leishmaniasis in a 4.5-month-old infant. *Rev Soc Bras Med Trop* 2012; 45: 407-409.
- 104) CELIK U, ALABAZ D, ALHAN E, BAYRAM I, CELIK T. Diagnostic dilemma in an adolescent boy: hemophagocytic syndrome in association with kala azar. *Am J Med Sci* 2007; 334: 139-141.
- 105) KOCAK N, EREN M, YUCE A, GUMRUK F. Hemophagocytic syndrome associated with visceral leishmaniasis. *Indian Pediatr* 2004; 41: 605-607.
- 106) TAPISIZ A, BELET N, CIFTCI E, INCE E, DOGRU U. Hemophagocytic lymphohistiocytosis associated with visceral leishmaniasis. *J Trop Pediatr* 2007; 53: 359-361.
- 107) TUNC B, AYATA A. Hemophagocytic syndrome: a rare life-threatening complication of visceral leishmaniasis in a young boy. *Pediatr Hematol Oncol* 2001; 18: 531-536.
- 108) OZYUREK E, OZCAY F, YILMAZ B, OZBEK N. Hemophagocytic lymphohistiocytosis associated with visceral leishmaniasis: a case report. *Pediatr Hematol Oncol* 2005; 22: 409-414.
- 109) GURGEY A, SECMEER G, TAVIL B, CEYHAN M, KUSKONMAZ B, CENGIZ B, OZEN H, KARA A, CETIN M, GUMRUK F. Secondary hemophagocytic lymphohistiocytosis in Turkish children. *Pediatr Infect Dis J* 2005; 24: 1116-1117.
- 110) SIPAHI T, TAVIL B, OKSAL A. Visceral leishmaniasis and pseudomonas septicemia associated with hemophagocytic syndrome and myelodysplasia in a Turkish child. *Turk J Pediatr* 2005; 47: 191-194.
- 111) KONTOPOULOU T, TSAOUSIS G, VAIDAKIS E, FANOURGIAKIS P, MICHALAKEAS E, TRIGONI E, SAMARKOS M. Hemophagocytic syndrome in association with visceral leishmaniasis. *Am J Med* 2002; 113: 439-440.
- 112) KOLIOU MG, SOTERIADES ES, EPHROS M, MAZERIS A, ANTONIOU M, ELIA A, NOVELLI V. Hemophagocytic lymphohistiocytosis associated with Epstein Barr virus and Leishmania donovani coinfection in a child from Cyprus. *J Pediatr Hematol Oncol* 2008; 30: 704-707.
- 113) MAROM D, OFFER I, TAMARY H, JAFFE CL, GARTY BZ. Hemophagocytic lymphohistiocytosis associated with visceral leishmaniasis. *Pediatr Hematol Oncol* 2001; 18: 65-70.
- 114) LEVY L, NASEREDDIN A, RAV-ACHA M, KEDMI M, RUND D, GATT ME. Prolonged fever, hepatosplenomegaly, and pancytopenia in a 46-year-old woman. *PLoS Med* 2009; 6: e1000053.
- 115) THABET F, TABARKI B, FEHEM R, YACCOUB M, SELMI H, ESSOUSSI AS. Syndrome of inappropriate macrophage activation associated with infantile visceral leishmaniasis. *Tunis Med* 1999; 77: 648-650.
- 116) NADRID A, POUSSE H, LARADI-CHEBIL S, KHELIF A, BEJAOU M, BESBES A, RADHOUANE M, GUEDICHE MN. Infantile visceral leishmaniasis: difficult diagnosis in cases complicated by hemophagocytosis. *Arch Pediatr* 1996; 3: 881-883.
- 117) KILANI B, AMMARI L, KANOUN F, BEN CHAABANE T, ABDELLATIF S, CHAKER E. Hemophagocytic syndrome associated with visceral leishmaniasis. *Int J Infect Dis* 2006; 10: 85-86.
- 118) BOUGUILA J, CHABCHOUB I, MONCEF Y, MLIKA A, SAGHROUNI F, BOUGHAMOURA L, ESSOUSSI AS. Treatment of severe hemophagocytic syndrome associated with visceral leishmaniasis. *Arch Pediatr* 2010; 17: 1566-1570.
- 119) SKRAM MK, BJERING S, HERMANSEN NO, DINI L, HELLEBOSTAD M. A 15-month-old girl with fever and pancytopenia. *Tidsskr Nor Laegeforen* 2011; 131: 2482-2486.
- 120) SUKOVA M, STARY J, HOUSKOVA J, NOHYNKOVA E. Hemophagocytic lymphohistiocytosis as a manifestation of visceral leishmaniasis. *Cas Lek Cesk* 2002; 141: 581-584.
- 121) SOTOCA FERNANDEZ JV, GARCIA VILLAESCUSA L, LILLO LILLO M, GARCIA MIALDEA O, CARRASCOSA ROMERO MC, TEBAR GIL R. Hemophagocytic syndrome secondary to visceral leishmaniasis. *An Pediatr (Barc)* 2008; 69: 46-48.
- 122) SANTAMARIA M, CARRILLO J, PEREZ-NAVERO J, MATEOS E, IBARRA I, FERNANDEZ S, ORTEGA C. Leishmaniasis and concurrent hemophagocytosis with or without transient perforin expression perturbation. *Pediatr Blood Cancer* 2008; 51: 310.
- 123) RODRIGUEZ-CUARTEIRO A, SALAS-GALAN A, PEREZ-GALVEZ MN, PEREZ-BLANCO FJ. Haemophagocytic visceral kala azar. *Infection* 1991; 19: 184.

- 124) NAVARRO DM, PEREZ BARRACHINA MC, GIRALT M. Visceral leishmaniasis and hemophagocytosis. *Sangre (Barc)* 1986; 31: 372-374.
- 125) CERDAN VERA MT, BERNAL FERRER AM, SEQUI CANET JM, SIFRE ARANDA M. Pericardial effusion in a case of hemophagocytic lymphohistiocytosis secondary to leishmaniasis. *An Pediatr (Barc)* 2012. doi.org/10.1016/j.anpedi.2012.05.011
- 126) MOLTO A, MATEO L, LLOVERAS N, OLIVE A, MINGUEZ S. Visceral leishmaniasis and macrophagic activation syndrome in a patient with rheumatoid arthritis under treatment with adalimumab. *Joint Bone Spine* 2010; 77: 271-273.
- 127) RUIZ GINES MA, RUIZ GINES JA, MENENDEZ GOMEZ JL, PEREZ COGOLLUDO AM, DOMINGUEZ MARTIN S, FERNANDEZ RODRIGUEZ E. Visceral leishmaniasis and bronchial asthma: influence of steroid therapy in the development of the macrophage activation syndrome and relative adrenal insufficiency. *An Med Interna* 2008; 25: 279-283.
- 128) BESSIS D, SOTTO A, TAIB J, CIURANA AJ. Photo quiz. Visceral leishmaniasis with hemophagocytic syndrome. *Clin Infect Dis* 1993; 17: 611, 829.
- 129) LAZANAS M, PERRONNE C, LOMVERDOS D, GALARIOTIS C, ARAPAKIS G, VILDE JL. Visceral leishmaniasis disclosed by histiocytosis with erythrophagocytosis. *Presse Med* 1990; 19: 765.
- 130) MICHEL G, SIMONIN G, PERRIMOND H, COIGNET J. Syndrome of activation of the mononuclear phagocyte system. Initial manifestation of visceral leishmaniasis. *Arch Fr Pediatr* 1988; 45: 45-46.
- 131) GAGNAIRE MH, GALAMBRUN C, STEPHAN JL. Hemophagocytic syndrome: A misleading complication of visceral leishmaniasis in children--a series of 12 cases. *Pediatrics* 2000; 106: E58.
- 132) ARSLAN F, BATIREL A, RAMAZAN M, OZER S, MERT A. Macrophage activation syndrome triggered by primary disseminated toxoplasmosis. *Scand J Infect Dis* 2012. doi:10.3109/00365548.2012.691208
- 133) BRIAND PY, GANGNEUX JP, FAVARETTO G, LY-SUN-NARAM B, GODARD M, ROBERT-GANGNEUX F, FEST T. Hemophagocytic syndrome and toxoplasmic primo-infection. *Ann Biol Clin (Paris)* 2008; 66: 199-205.
- 134) HEBRAUD B, KAMAR N, BORDE JS, BESSIERES MH, GALINIER M, ROSTAING L. Unusual presentation of primary toxoplasmosis infection in a kidney-transplant patient complicated by an acute left-ventricular failure. *NDT Plus* 2008; 1: 429-432.
- 135) SEGALL L, MOAL MC, DOUCET L, KERGOAT N, BOURBIGOT B. Toxoplasmosis-associated hemophagocytic syndrome in renal transplantation. *Transpl Int* 2006; 19: 78-80.
- 136) DUBAND S, CORNILLON J, TAVERNIER E, DUMOLLARD JM, GUYOTAT D, PEOC'H M. Toxoplasmosis with hemophagocytic syndrome after bone marrow transplantation: diagnosis at autopsy. *Transpl Infect Dis* 2008; 10: 372-374.
- 137) GUILLAUME MP, DRIESENS N, LIBERT M, DE BELS D, CORAZZA F, KARMAI R. Hemophagocytic syndrome associated with extracerebral toxoplasmosis in an HIV-infected patient. *Eur J Intern Med* 2006; 17: 503-504.
- 138) Blanche P, Robert F, Dupouy-Camet J, Sicard D. Toxoplasmosis-associated hemophagocytic syndrome in a patient with AIDS: diagnosis by the polymerase chain reaction. *Clin Infect Dis* 1994; 19: 989-990.
- 139) MAJLUF-CRUZ AS, HURTADO MONROY R, SOUTO-MEIRINO C, DEL RIO CHIRIBOGA C, SIMON J. Hemophagocytic syndrome associated with histoplasmosis in the acquired immunodeficiency syndrome: description of 3 cases and review of the literature. *Sangre (Barc)* 1993; 38: 51-55.
- 140) NUMATA K, TSUTSUMI H, WAKAI S, TACHI N, CHIBA S. A child case of haemophagocytic syndrome associated with cryptococcal meningoencephalitis. *J Infect* 1998; 36: 118-119.
- 141) CHANDRA H, CHANDRA S, SHARMA A. Histoplasmosis on bone marrow aspirate cytological examination associated with hemophagocytosis and pancytopenia in an AIDS patient. *Korean J Hematol* 2012; 47: 77-79.
- 142) VAID N, PATEL P. A case of haemophagocytic syndrome in HIV-associated disseminated histoplasmosis. *Acute Med* 2011; 10: 142-144.
- 143) PANDE A, BHATTACHARYYA M, PAIN S, GHOSH A, SAMANTA A. Diagnostic yield of bone marrow examination in HIV associated FUO in ART naive patients. *J Infect Public Health* 2010; 3: 124-129.
- 144) SANCHEZ A, CELAYA AK, VICTORIO A. Histoplasmosis-associated hemophagocytic syndrome: a case report. *AIDS Read* 2007; 17: 496-499.
- 145) GUIOT HM, BERTRAN-PASARELL J, TORMOS LM, GONZALEZ-KEELAN C, PROCOP GW, FRADERA J, SANCHEZ-SERGENTON C, MENDEZ W. Ileal perforation and reactive hemophagocytic syndrome in a patient with disseminated histoplasmosis: the role of the real-time polymerase chain reaction in the diagnosis and successful treatment with amphotericin B lipid complex. *Diagn Microbiol Infect Dis* 2007; 57: 429-433.
- 146) GIL-BRUSOLA A, PEMAN J, SANTOS M, SALAVERT M, LACRUZ J, GOBERNADO M. Disseminated histoplasmosis with hemophagocytic syndrome in a patient with AIDS: description of one case and review of the Spanish literature. *Rev Iberoam Micol* 2007; 24: 312-316.
- 147) KODURI PR, CHUNDI V, DEMARAIS P, MIZOCK BA, PATEL AR, WEINSTEIN RA. Reactive hemophagocytic syndrome: a new presentation of disseminated histoplasmosis in patients with AIDS. *Clin Infect Dis* 1995; 21: 1463-1465.
- 148) MADRIGAL-JIMENEZ HM, HERNANDEZ-RIVERA G. Usefulness of bone marrow microscopic examination in HIV-infected patients with pancytopenia. *Gac Med Mex* 2006; 142: 13-17.
- 149) KHANDEKAR MM, DESHMUKH SD, HOLLA VV, RANE SR, KAKRANI AL, SANGALE SA, HABBU AA, PANDIT DP, BHORE AV, SASTRY J, PHADKE MA, BOLLINGER RC. Profile of bone marrow examination in HIV/AIDS patients to detect opportunistic infections, especial-

- ly tuberculosis. *Indian J Pathol Microbiol* 2005; 48: 7-12.
- 150) DE LAVAISSIERE M, MANCERON V, BOUREE P, GARCON L, BISARO F, DELFRAISSY JF, LAMBOTTE O, GOJJARD C. Reconstitution inflammatory syndrome related to histoplasmosis, with a hemophagocytic syndrome in HIV infection. *J Infect* 2009; 58: 245-247.
 - 151) QUIJANO G, SIMINOVICH M, DRUT R. Histopathologic findings in the lymphoid and reticuloendothelial system in pediatric HIV infection: a postmortem study. *Pediatr Pathol Lab Med* 1997; 17: 845-856.
 - 152) VAN KOEVERINGE MP, BROUWER RE. Histoplasma capsulatum reactivation with haemophagocytic syndrome in a patient with chronic lymphocytic leukaemia. *Neth J Med* 2010; 68: 418-421.
 - 153) RAO RD, MORICE WG, PHYLIKY RL. Hemophagocytosis in a patient with chronic lymphocytic leukemia and histoplasmosis. *Mayo Clin Proc* 2002; 77: 287-290.
 - 154) MEHTA BM, HASHKES PJ, AVERY R, DEAL CL. A 21-year-old man with Still's disease with fever, rash, and pancytopenia. *Arthritis Care Res (Hoboken)* 2010; 62: 575-579.
 - 155) JAYAKAR BA, HASHKES PJ. Macrophage activation syndrome: why and what should a gastroenterologist know. *J Clin Gastroenterol* 2011; 45: 210-214.
 - 156) AGARWAL S, MOODLEY J, AJANI GOEL G, THEIL KS, MAHMOOD SS, LANG RS. A rare trigger for macrophage activation syndrome. *Rheumatol Int* 2009; 31: 405-407.
 - 157) LO MM, MO JQ, DIXON BP, CZECH KA. Disseminated histoplasmosis associated with hemophagocytic lymphohistiocytosis in kidney transplant recipients. *Am J Transplant* 2010; 10: 687-691.
 - 158) MASRI K, MAHON N, ROSARIO A, MIRZA I, KEYS TF, RATLIFF NB, STARLING RC. Reactive hemophagocytic syndrome associated with disseminated histoplasmosis in a heart transplant recipient. *J Heart Lung Transplant* 2003; 22: 487-491.
 - 159) KELLER FG, KURTZBERG J. Disseminated histoplasmosis: a cause of infection-associated hemophagocytic syndrome. *Am J Pediatr Hematol Oncol* 1994; 16: 368-371.
 - 160) PHILLIPS J, STASZEWSKI H, GARRISON M. Successful treatment of secondary hemophagocytic lymphohistiocytosis in a patient with disseminated histoplasmosis. *Hematology* 2008; 13: 282-285.
 - 161) CHEMLAL K, ANDRIEU-BAUTRU V, COUVELARD A. Hemophagocytic syndrome during *Histoplasma capsulatum* infection. *Haematologica* 1997; 82: 726.
 - 162) SALUJA S, SUNITA, BHASIN S, GUPTA DK, GUPTA B, KATARIA SP, SHARMA M. Disseminated histoplasmosis with reactive haemophagocytosis presenting as POU in an immunocompetent host. *J Assoc Physicians India* 2005; 53: 906-907.
 - 163) KUMAR N, JAIN S, SINGH ZN. Disseminated histoplasmosis with reactive hemophagocytosis: aspiration cytology findings in two cases. *Diagn Cytopathol* 2000; 23: 422-424.
 - 164) WANG Z, DUARTE AG, SCHNADIG VJ. Fatal reactive hemophagocytosis related to disseminated histoplasmosis with endocarditis: an unusual case diagnosed at autopsy. *South Med J* 2007; 100: 208-211.
 - 165) PEI SN, LEE CH, LIU JW. Hemophagocytic syndrome in a patient with acquired immunodeficiency syndrome and acute disseminated penicilliosis. *Am J Trop Med Hyg* 2008; 78: 11-13.
 - 166) CHOKEPHAIBULKIT K, VEERAKUL G, VANPRAPAR N, CHAIPRASERT A, TANPHAICHITR V, CHEARSKUL S. Penicilliosis-associated hemophagocytic syndrome in a human immunodeficiency virus-infected child: the first case report in children. *J Med Assoc Thai* 2001; 84: 426-429.
 - 167) VEERAKUL G, SANPAKIT K, TANPHAICHITR VS, MAHASANDANA C, JIRARATTANASOPA N. Secondary hemophagocytic lymphohistiocytosis in children: an analysis of etiology and outcome. *J Med Assoc Thai* 2002; 85 Suppl 2: S530-541.
 - 168) CHIM CS, FONG CY, MA SK, WONG SS, YUEN KY. Reactive hemophagocytic syndrome associated with *Penicillium marneffe* infection. *Am J Med* 1998; 104: 196-197.
 - 169) VECSEI AK, KASTNER U, TREBO M, KORNMULLER R, PICHER O, SCHRATZBERGER-VECSEI E, GADNER H. Pediatric visceral leishmaniasis in Austria: diagnostic difficulties in a non-endemic region. *Wien Klin Wochenschr* 2001; 113: 102-106.
 - 170) PAPPAS G. Of mice and men: defining, categorizing and understanding the significance of zoonotic infections. *Clin Microbiol Infect* 2011; 17: 321-325.
 - 171) NG WF, TO KF, LAM WW, NG TK, LEE KC. The comparative pathology of severe acute respiratory syndrome and avian influenza A subtype H5N1--a review. *Hum Pathol* 2006; 37: 381-390.
 - 172) HARMS PW, SCHMIDT LA, SMITH LB, NEWTON DW, PLETNEVA MA, WALTERS LL, TOMLINS SA, FISHER-HUBBARD A, NAPOLITANO LM, PARK PK, BLAIVAS M, FANTONE J, MYERS JL, JENTZEN JM. Autopsy findings in eight patients with fatal H1N1 influenza. *Am J Clin Pathol* 2010; 134: 27-35.
 - 173) ROUPHAEL NG, TALATI NJ, VAUGHAN C, CUNNINGHAM K, MOREIRA R, GOULD C. Infections associated with haemophagocytic syndrome. *Lancet Infect Dis* 2007; 7: 814-822.
 - 174) CASCIO A, TODARO G, BONINA L, IARIA C. Please, do not forget secondary hemophagocytic lymphohistiocytosis in HIV-infected patients. *Int J Infect Dis* 2011; 15: e885-886.
 - 175) TAKAHASHI S, OKI J, MIYAMOTO A, KOYANO S, ITO K, AZUMA H, OKUNO A. Encephalopathy associated with haemophagocytic lymphohistiocytosis following rotavirus infection. *Eur J Pediatr* 1999; 158: 133-137.
 - 176) ARISTA S, VIZZI E, FERRARO D, CASCIO A, DI STEFANO R. Distribution of VP7 serotypes and VP4 genotypes among rotavirus strains recovered from

- Italian children with diarrhea. *Arch Virol* 1997; 142: 2065-2071.
- 177) CASCIO A, VIZZI E, ALAIMO C, ARISTA S. Rotavirus gastroenteritis in Italian children: can severity of symptoms be related to the infecting virus? *Clin Infect Dis* 2001; 32: 1126-1132.
- 178) ARISTA S, GIAMMANCO GM, DE GRAZIA S, MIGLIORE MC, MARTELLA V, CASCIO A. Molecular characterization of the genotype G9 human rotavirus strains recovered in Palermo, Italy, during the winter of 1999-2000. *Epidemiol Infect* 2004; 132: 343-349.
- 179) ARISTA S, VIZZI E, MIGLIORE MC, DI ROSA E, CASCIO A. High incidence of G9P181 rotavirus infections in Italian children during the winter season 1999-2000. *Eur J Epidemiol* 2003; 18: 711-714.
- 180) ARISTA S, VIZZI E, ALAIMO C, PALERMO D, CASCIO A. Identification of human rotavirus strains with the P[14] genotype by PCR. *J Clin Microbiol* 1999; 37: 2706-2708.
- 181) LUCHS A, CILLI A, MORILLO SG, CARMONA RDE C, Timenetsky Mdo C. Rare G3P[3] rotavirus strain detected in Brazil: possible human-canine interspecies transmission. *J Clin Virol* 2012; 54: 89-92.
- 182) DE GRAZIA S, MARTELLA V, GIAMMANCO GM, GOMARA MI, RAMIREZ S, CASCIO A, COLOMBA C, ARISTA S. Canine-origin G3P[3] rotavirus strain in child with acute gastroenteritis. *Emerg Infect Dis* 2007; 13: 1091-1093.
- 183) DAVID A, IARIA C, GIORDANO S, IARIA M, CASCIO A. Secondary hemophagocytic lymphohistiocytosis: forget me not! *Transpl Infect Dis* 2012. DOI: 10.1111/j.1399-3062.2012.00770.x
- 184) BENEDETTO F, LENTINI S, PASSARI G, STILO F, DE CARIDI G, CASCIO A, SPINELLI F. Endovascular repair of aortic rupture due to *Brucella* aortitis. *Vasa* 2011; 40: 150-156.
- 185) ARIZA J, BOSILKOVSKI M, CASCIO A, COLMENERO JD, CORBEL MJ, FALAGAS ME, MEMISH ZA, ROUSHAN MR, RUBINSTEIN E, SIPSAS NV, SOLERA J, YOUNG EJ, PAPPAS G. Perspectives for the treatment of brucellosis in the 21st century: the Ioannina recommendations. *PLoS Med* 2007; 4: e317.
- 186) CASCIO A, DI LIBERTO C, D'ANGELO M, IARIA C, SCARLATA F, TITONE L, CAMPISI G. No findings of dental defects in children treated with minocycline. *Antimicrob Agents Chemother* 2004; 48: 2739-2741.
- 187) CASCIO A, SCARLATA F, GIORDANO S, ANTINORI S, COLOMBA C, TITONE L. Treatment of human brucellosis with rifampin plus minocycline. *J Chemother* 2003; 15: 248-252.
- 188) CASCIO A, MAGGIO MC, CARDELLA F, ZANGARA V, ACCOMANDO S, COSTA A, IARIA C, MANSUETO P, GIORDANO S. Coronary involvement in Mediterranean spotted fever. *New Microbiol* 2011; 34: 421-424.
- 189) CASCIO A, IARIA C. Epidemiology and clinical features of Mediterranean spotted fever in Italy. *Parassitologia* 2006; 48: 131-133.
- 190) CASCIO A, COLOMBA C, ANTINORI S, PATERSON DL, TITONE L. Clarithromycin versus azithromycin in the treatment of Mediterranean spotted fever in children: a randomized controlled trial. *Clin Infect Dis* 2002; 34: 154-158.
- 191) CASCIO A, DONES P, ROMANO A, TITONE L. Clinical and laboratory findings of boutonniere fever in Sicilian children. *Eur J Pediatr* 1998; 157: 482-486.
- 192) CASCIO A, COLOMBA C. [Macrolides in the treatment of children with Mediterranean spotted fever]. *Infez Med* 2002; 10: 145-150.
- 193) CASCIO A, COLOMBA C, DI ROSA D, SALSA L, DI MARTINO L, TITONE L. Efficacy and safety of clarithromycin as treatment for Mediterranean spotted fever in children: a randomized controlled trial. *Clin Infect Dis* 2001; 33: 409-411.
- 194) CASCIO A, GERVASI F, GIORDANO S, PALAZZOLO B, SALSA L. Plasma levels of tumor necrosis factor-alpha and interferon-gamma in Sicilian children with Mediterranean spotted fever. *Int J Clin Lab Res* 1997; 27: 135-138.
- 195) PARMENTIER B, HAMMEL P, BENNANI H, VALLA D, LEVY P, RUSZKIEWSKI P. Severe thrombopenia as single sign of hemophagocytosis in a patient with cirrhosis and lethal infection of ascitic fluid by *Escherichia coli*. *Gastroenterol Clin Biol* 2007; 31: 967-969.
- 196) PINZONE MR, CELESIA BM, DI ROSA M, CACOPARDO B, NUNNARI G. Microbial translocation in chronic liver diseases. *Int J Microbiol* 2012; 2012: 694629. doi: 10.1155/2012/694629
- 197) CASCIO A, STASSI G, CACCIOLA I, SAITTA C, SQUADRITO G. Fever and rhomboid target lesion in decompensated cirrhosis. *Lancet Infect Dis* 2012; 12: 576.
- 198) PITINI V, CASCIO A, ARRIGO C, ALTAVILLA G. Visceral leishmaniasis after alemtuzumab in a patient with chronic lymphocytic leukaemia. *Br J Haematol* 2012; 156: 1.
- 199) SIMON I, WISSING KM, DEL MARMOL V, ANTINORI S, REMMELINK M, NILUFER BROEDERS E, NORTIER JL, CORBELLINO M, ABRAMOWICZ D, CASCIO A. Recurrent leishmaniasis in kidney transplant recipients: report of 2 cases and systematic review of the literature. *Transpl Infect Dis* 2011; 13: 397-406.
- 200) CASCIO A, IARIA M, IARIA C. Leishmaniasis and biologic therapies for rheumatologic diseases. *Semin Arthritis Rheum* 2010; 40: e3-5.
- 201) ANTINORI S, CASCIO A, PARRAVICINI C, BIANCHI R, CORBELLINO M. Leishmaniasis among organ transplant recipients. *Lancet Infect Dis* 2008; 8: 191-199.
- 202) CASCIO A, IARIA C, ANTINORI S. Visceral leishmaniasis as a cause of anemia in HIV-infected patients. *Clin Infect Dis* 2004; 39: 1088-1089.
- 203) CASCIO A, COLOMBA C. Childhood Mediterranean visceral leishmaniasis. *Infez Med* 2003; 11: 5-10.
- 204) CASCIO A, COLOMBA C, ANTINORI S, OROBELLO M, PATERSON D, TITONE L. Pediatric visceral leishmaniasis in Western Sicily, Italy: a retrospective analysis of 111 cases. *Eur J Clin Microbiol Infect Dis* 2002; 21: 277-282.

- 205) CASCIO A, GRADONI L, SCARLATA F, GRAMICCIA M, GIORDANO S, RUSSO R, SCALONE A, CAMMA C, TITONE L. Epidemiologic surveillance of visceral leishmaniasis in Sicily, Italy. *Am J Trop Med Hyg* 1997; 57: 75-78.
- 206) CASCIO A, IARIA C. Appropriate screening for leishmaniasis before immunosuppressive treatments. *Emerg Infect Dis* 2009; 15: 1706; author reply 1706-1707.
- 207) ANTINORI S, CALATTINI S, PIOLINI R, LONGHI E, BESTETTI G, CASCIO A, PARRAVICINI C, CORBELLINO M. Is real-time polymerase chain reaction (PCR) more useful than a conventional PCR for the clinical management of leishmaniasis? *Am J Trop Med Hyg* 2009; 81: 46-51.
- 208) ANTINORI S, CALATTINI S, LONGHI E, BESTETTI G, PIOLINI R, MAGNI C, ORLANDO G, GRAMICCIA M, ACQUAVIVA V, FOSCHI A, CORVASCE S, COLOMBA C, TITONE L, PARRAVICINI C, CASCIO A, CORBELLINO M. Clinical use of polymerase chain reaction performed on peripheral blood and bone marrow samples for the diagnosis and monitoring of visceral leishmaniasis in HIV-infected and HIV-uninfected patients: a single-center, 8-year experience in Italy and review of the literature. *Clin Infect Dis* 2007; 44: 1602-1610.
- 209) CASCIO A, CALATTINI S, COLOMBA C, SCALAMOGNA C, GALAZZI M, PIZZUTO M, CAMILLI R, GRAMICCIA M, TITONE L, CORBELLINO M, ANTINORI S. Polymerase chain reaction in the diagnosis and prognosis of Mediterranean visceral leishmaniasis in immunocompetent children. *Pediatrics* 2002; 109: E27.
- 210) CASCIO A, DI MARTINO L, OCCORSIO P, GIACCHINO R, CATANIA S, GIGLIOTTI AR, AIASSA C, IARIA C, GIORDANO S, COLOMBA C, POLARA VF, TITONE L, GRADONI L, GRAMICCIA M, ANTINORI S. A 6 day course of liposomal amphotericin B in the treatment of infantile visceral leishmaniasis: the Italian experience. *J Antimicrob Chemother* 2004; 54: 217-220.
- 211) DI MARTINO L, DAVIDSON RN, GIACCHINO R, SCOTTI S, RAIMONDI F, CASTAGNOLA E, TASSO L, CASCIO A, GRADONI L, GRAMICCIA M, PETTOELLO-MANTOVANI M, BRYCESON AD. Treatment of visceral leishmaniasis in children with liposomal amphotericin B. *J Pediatr* 1997; 131: 271-277.
- 212) DAVIDSON RN, DI MARTINO L, GRADONI L, GIACCHINO R, GAETA GB, PEMPINELLO R, SCOTTI S, CASCIO A, CASTAGNOLA E, MAISTO A, GRAMICCIA M, DI CAPRIO D, WILKINSON RJ, BRYCESON AD. Short-course treatment of visceral leishmaniasis with liposomal amphotericin B (AmBisome). *Clin Infect Dis* 1996; 22: 938-943.
- 213) CASTAGNOLA E, DAVIDSON RN, FIORE P, TASSO L, ROSSI G, MANGRAVITI S, DI MARTINO L, SCOTTI S, CASCIO A, PEMPINELLO R, GRADONI L, GIACCHINO R. Early efficacy of liposomal amphotericin B in the treatment of visceral leishmaniasis. *Trans R Soc Trop Med Hyg* 1996; 90: 317-318.
- 214) DAVIDSON RN, DI MARTINO L, GRADONI L, GIACCHINO R, RUSSO R, GAETA GB, PEMPINELLO R, SCOTT S, RAIMONDI F, CASCIO A, ET AL. Liposomal amphotericin B (AmBisome) in Mediterranean visceral leishmaniasis: a multi-centre trial. *Q J Med* 1994; 87: 75-81.
- 215) IARIA C, LEONARDI MS, BUDA A, TORO ML, CASCIO A. Measles and secondary hemophagocytic lymphohistiocytosis. *Emerg Infect Dis* 2012; 18: 1529a-1529.
- 216) CASCIO A, IARIA C, RUGGERI P, FRIES W. Cytomegalovirus pneumonia in patients with inflammatory bowel disease: a systematic review. *Int J Infect Dis* 2012; 16: e474-479.
- 217) LO PRESTI MA, COSTANTINO G, DELLA TORRE A, BELVEDERE A, CASCIO A, FRIES W. Severe CMV-related pneumonia complicated by the hemophagocytic lymphohistiocytic (HLH) syndrome in quiescent Crohn's colitis: harmful cure? *Inflamm Bowel Dis* 2011; 17: E145-146.
- 218) CASCIO A, IARIA C, RICCIARDI F, FRIES W. Comment to "Management of cytomegalovirus infection in inflammatory bowel diseases". *Dig Liver Dis* 2012. doi.org/10.1016/j.dld.2012.07.015
- 219) KELEKÇI S, EVLIYAO LU O, SEN V, YOLBA I, ULUCA U, TAN I, GÜRKAN MF. The relationships between clinical outcome and the levels of total antioxidant capacity (TAC) and coenzyme Q (CoQ 10) in children with pandemic influenza (H 1 N1) and seasonal flu. *Eur Rev Med Pharmacol Sci*. 2012; 16: 1033-1038.
- 220) HU R. Separating the chaff from the grain (Tularemia). *Eur Rev Med Pharmacol Sci* 2012; 16: 554-558.
- 221) GUPTA A, TYRRELL P, VALANI R, BENSELER S, WEITZMAN S, ABDELHALEEM M. The role of the initial bone marrow aspirate in the diagnosis of hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2008; 51: 402-404.
- 222) FREEMAN B, RATHORE MH, SALMAN E, JOYCE MJ, PITEL P. Intravenously administered immune globulin for the treatment of infection-associated hemophagocytic syndrome. *J Pediatr* 1993; 123: 479-481.
- 223) WANG S, DEGAR BA, ZIESKE A, SHAFI NQ, ROSE MG. Hemophagocytosis exacerbated by G-CSF/GM-CSF treatment in a patient with myelodysplasia. *Am J Hematol* 2004; 77: 391-396.