

Vaccination practice in children with rheumatic disease

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ABSTRACT

Introduction/Objectives: Evaluate clinical practice through assessment of vaccination card and recommendation of specific vaccines in pediatric patients with rheumatic diseases in use of different drugs and reveal the possible association between vaccination frequency and time of the clinical practice of pediatric rheumatologists in the state of São Paulo.

Material and Methods: A questionnaire was sent to pediatric rheumatologists of the *Departamento de Reumatologia da Sociedade de Pediatria de São Paulo*. This instrument included questions about practice time on Pediatric Rheumatology, vaccination of patients with juvenile systemic lupus erythematosus (JSLE), juvenile idiopathic arthritis (JIA), juvenile dermatomyositis (JDM), and immunization according to the treatments used. **Results:** Vaccination card was seen by 100% of the professionals at the first visit and by 36% annually. Vaccines of live agents were not recommended for patients with JSLE, JIA, and JDM in 44%, 64%, and 48%, respectively. The professionals were divided into two groups: Group A (≤ 15 years of practice, $n = 12$) and B (≥ 16 years, $n = 13$). No statistical difference was observed in the use of live agent vaccine and vaccines with inactivated agents or protein components in the two treatment groups ($P > 0.05$). Moreover, the groups had similar opinion regarding severity of immunosuppression in patients with JSLE, JIA, and JDM (with or without activity) and treatment used ($P > 0.05$). **Conclusions:** The frequency of immunization by pediatric rheumatologists in São Paulo is low, especially after the first visit, and not influenced by time of professional practice.

Keywords: vaccination, children, systemic lupus erythematosus, juvenile idiopathic arthritis, rheumatic disease.

INTRODUCTION

Infections are a major cause of morbidity and mortality in Brazilian children and teenagers with chronic rheumatic diseases. In some children, particularly those with systemic lupus erythematosus (JSLE),^{1,2} juvenile idiopathic arthritis (JIA), and juvenile dermatomyositis (JDM),³ not only the treatment used but the disease itself establishes a state of immunosuppression.

One of the preventive measures against infectious disease is passive immunization.⁴⁻⁶ The primary vaccination

schedule is applied especially during childhood and adolescence, the age group with the highest prevalence of certain rheumatic diseases. Although inactivated vaccines agents have proved generally safe in patients with rheumatic diseases, some studies in adults have shown activation of disease after vaccination.⁷ Furthermore, vaccines may not induce adequate immunogenicity in patients using potentially immunosuppressive drugs. Recently, our concern with these issues was highlighted in a systematic review of medical literature on efficacy and safety of vaccines in children and adolescents with rheumatic diseases based on

Received on 04/06/2009. Approved on 05/30/2010. We declare no conflict of interest.

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levels of scientific evidence.⁸ This consensus demonstrated the safety and efficacy of inactivated vaccines and protein components against virus, such as hepatitis A and B, *influenza*, pneumococcus, meningococcus, *Haemophilus*, Salk, and tetanus, in patients with rheumatic diseases, despite the use of immunosuppressive drugs. Furthermore, this review suggested that vaccination with live agents against yellow fever, BCG, rotavirus, varicella, polio, and MMR are contraindicated in immunosuppressed patients.

However, few studies have assessed the clinical practice of pediatric rheumatologists in immunization of these diseases. Davies & Woo forwarded a questionnaire to members of the English Group of Pediatric Rheumatology and observed inconsistency in immunization practice among specialists from different British services.⁹

The time of clinical practice allows more opportunity to comment on vaccination considering protection and risk in a larger number of patients with rheumatic diseases. Furthermore, over time, there was refinement in vaccination practice with better knowledge and greater availability of vaccines, especially with the emergence of Reference Centers of Special Immunobiologic Products.

Study evaluating the immunization practice according to the years of practice has not been done. The objective of this study was to evaluate the clinical practice of vaccinations recommended by pediatric rheumatologists in the state of São Paulo for children and adolescents with rheumatic diseases, similar to the British study, and to reveal a possible association between increased frequency of immunization prescription by professionals and longer practice in the specialty.

MATERIAL AND METHODS

During April of 2009, a questionnaire on immunization practices was sent by e-mail to 26 pediatric rheumatologists of *Departamento de Reumatologia Pediátrica da Sociedade de Pediatria de São Paulo (SPSP)*. This questionnaire was sent three times consecutively within two weeks. Of the 26 professionals, 25 (96%) answered the questionnaire. All medical specialists have qualification certificate in Pediatric Rheumatology and/or Rheumatology and act in daily teaching activities, care, and research.

The questionnaire included open questions and issues related to immunization practice. Some of these questions were modified from Davies & Woo⁹ (questions 5 and 6). The following open questions were included:

- How long (in years) have you been practicing pediatric rheumatology?

- Which vaccines are routinely recommended (when there is no contraindication) to patients with JSLE (American College of Rheumatology classification criteria),¹⁰ JIA (International League of Associations for Rheumatology classification criteria),¹¹ and JDM (Bohan & Peter classification criteria)?¹²
- The vaccination card is seen at the first visit?
- How many times vaccination card is seen in follow-up?
- Personal opinion regarding the indication and contraindication of specific vaccines in patients with rheumatic diseases of childhood using different doses and combination drugs.

The frequency of recommendations of the following vaccines were assessed: inactivated vaccines and protein components [against hepatitis A and B, human papilloma virus (HPV), *influenza*, pneumococcal, meningococcal, tetanus and diphtheria toxoids, inactivated polio and *Haemophilus*] and live attenuated agent vaccines [against polio, measles, mumps and rubella (MMR), bacillus Calmette-Guerin (BCG), rotavirus, yellow fever, and chickenpox].

Treatments with prednisone at different doses (above or below 2 mg/kg/day) were evaluated and the use of the following drugs independent of doses: immunosuppressive (IS) and/or disease-modifying drugs (DMDs) [Methotrexate (MTX), antimalarials (chloroquine and hydroxychloroquine), sulfasalazine, leflunomide, azathioprine, cyclosporine, mycophenolate mofetil and cyclophosphamide] and biological agents.

- Personal opinion on the intensity of immunosuppression resulting from the use of corticosteroids (CT) at different doses, IS drugs and/or DMARDs [MTX in increasing doses, antimalarial drugs (chloroquine and hydroxychloroquine), sulfasalazine, leflunomide, azathioprine, cyclosporine, mycophenolate mofetil and cyclophosphamide] and biological agents in JIA, JDM, and JSLE diseases.

Later, participants were divided into two groups according to the median time (years) of pediatric rheumatology practice (from the first year of residency or internship in the specialty to April 30, 2009): group A (≤ 15 years of pediatric rheumatology practice) and group B (≥ 16 years of practice).

Statistical analysis

The time of clinical practice in pediatric rheumatology was presented as median (range), compared between groups A and B by Mann-Whitney test. Categorical variables were presented as number (%) and compared using Fisher exact test. The significance level of 5% ($P < 0.05$) was used for all statistical tests.

RESULTS

Table 1 shows the frequency of different vaccines recommendation for patients with JSLE, JIA, and JDM by the 25 professionals interviewed. Inactivated vaccines were recommended for all three diseases by over 50% of pediatric rheumatologists. There was an emphasis on vaccines not included in the basic schedule of immunizations, especially influenza vaccine (indicated by 76% of professionals) and pneumococcal (indicated by 84% of professionals to JSLE patients, 68% to JIA, and 72% to JDM).

The vaccination card was checked at the first visit by 100% of specialists and annually by just nine of 25 (36%). There was no statistical difference between the median time of pediatric rheumatology practice in the group that checked the immunization card every year and the group that did not have this behavior [15 (9-27) versus 19 (30-40) years, P = 0.91].

The frequency of vaccine indications by pediatric rheumatologists according to disease and treatment is shown in Table 2. Eighteen (72%) physicians reported the use of live agent vaccines, generally in patients with non-steroidal anti-inflammatory drugs (NSAIDs) or not using CT, MTX, or

Table 1
Vaccines routinely recommended by 25 pediatric rheumatologists according to disease

Vaccines	JSLE N (%)	JIA N (%)	JDM N (%)
dT or dTap*	18 (72)	18 (72)	18 (72)
SALK*	13 (52)	13 (52)	13 (52)
<i>Haemophilus</i> *	14 (56)	15 (60)	14 (56)
Influenza*	19 (76)	19 (76)	19 (76)
Pneumococcal*	21 (84)	17 (68)	18 (72)
Meningitis C*	16 (64)	15 (60)	15 (60)
Hepatitis A*	14 (56)	13 (52)	14 (56)
Hepatitis B*	14 (56)	14 (56)	18 (72)
MMR without CT and IS	3 (12)	8 (32)	3 (12)
MMR with CT < 2 mg/kg/day, without IS	5 (20)	5 (20)	4 (16)
Varicella without CT and IS	2 (8)	3 (12)	3 (12)
Varicella with CT < 2 mg/kg/day, without IS	2 (8)	3 (12)	3 (12)
Yellow fever without CT and IS	2 (8)	3 (12)	2 (8)
Yellow fever with CT < 2 mg/kg/day, without IS	2 (8)	1 (4)	2 (8)

JSLE = juvenile systemic lupus erythematosus; JIA = juvenile idiopathic arthritis; JDM = juvenile dermatomyositis; DPT = diphtheria, pertussis and tetanus; DTaP = acellular triple bacterial; CT = corticosteroids; IS = immunosuppressants.
* Vaccines given regardless of treatment used and disease activity.

other immunosuppressive drugs. Furthermore, 24 (96%) of professionals reported using inactivated vaccines in pediatric patients with rheumatic diseases in the same situations described above.

We evaluated the opinions of 25 professionals in accordance with the risk of infection or disease treatment. Regarding the risk of infection, JSLE in activity was considered as the rheumatic diseases of childhood that provides moderate to high risk of infection by most professionals (96%). Similarly, JDM and systemic JIA in activity were also considered to carry a high risk of infections (80% and 68%, respectively). The percentage of participants who considered moderate to severe risk of infection was proportional to the increased dose of corticosteroids (8% at doses below 0.2 mg/kg/day to 100% at doses above 2 mg/kg/day), which also occurred with the use of MTX. The IS (azathioprine, cyclophosphamide, and mycophenolate mofetil) and biological agents were considered drugs with high risk of serious infections.

The difference in practice time did not result in discrepancies in live or inactivated agent vaccine recommendations in general, according to treatment used (NSAIDs, CT, MTX, IS, and biological agents) by the two groups (P > 0.05; Table 3). Likewise, there was no statistical difference between the two groups regarding the level of immunosuppression assigned to rheumatic diseases of childhood with or without clinical activity (JSLE, JIA, and JDM) and treatment used (NSAIDs, CT, MTX, IS, and biological agents) (P > 0.05).

DISCUSSION

The present study demonstrates that the clinical practice regarding immunization is homogeneous among pediatric rheumatologists, despite the heterogeneity of practice time in the field. However, only about a third of the specialists have adequate surveillance of vaccine card after the first medical visit.

The two groups had very similar views regarding vaccine guidance and definition of serious risk of infections. Moreover, there was agreement on some of the responses in more than 80% of medical specialists. By definition, this high frequency between the two groups is considered a “consensus among experts”.¹³ In this research, there are doctors of various age groups that were formed in the same department of Pediatric Rheumatology by colleagues of various generations. This fact probably justifies the similarity of the medical practices. In addition, all participants work in university services, participate in continuing medical education, and most have post-graduate studies.

An important aspect, however, was the low standard indication by experts of vaccines against hepatitis A and B,

Table 2

Vaccines indicated by 25 pediatric rheumatologists according to treatment used

	With NSAIDs N (%)	Without MTX, IS, or CTN (%)	MTX or single IS N (%)	Prednisone < 2 mg/kg/day without MTX or IS N (%)	Prednisone < 2 mg/kg/day, with MTX or IS N (%)	Prednisone > 2 mg/kg/day without MTX or IS N (%)	Prednisone > 2 mg/kg/day with MTX or IS N (%)	With biological agents (anti-TNF, rituximab or abatacept) N (%)
Live agent vaccines in general	18 (72)	18 (72)	1 (4)	2 (8)	2 (8)	0 (0)	0 (0)	0 (0)
Inactive vaccines in general	24 (96)	24 (96)	23 (92)	22 (88)	20 (80)	19 (76)	19 (76)	18 (72)
Oral polio vaccine	20 (80)	19 (76)	2 (8)	4 (16)	2 (8)	1 (4)	1 (4)	1 (4)
MMR vaccine	22 (88)	21 (84)	3 (12)	6 (24)	2 (8)	1 (4)	1 (4)	1 (4)
BCG vaccine	20 (80)	19 (76)	1 (4)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)
Yellow fever vaccine	21 (84)	21 (84)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	0 (0)
Chickenpox vaccine	19 (76)	23 (92)	3 (12)	6 (24)	1 (4)	0 (0)	0 (0)	0 (0)
HPV vaccine	22 (88)	21 (84)	16 (64)	16 (64)	14 (56)	13 (52)	13 (52)	13 (52)
Meningococcal vaccine	25 (100)	24 (96)	22 (88)	21 (84)	19 (76)	18 (72)	18 (72)	18 (72)
Hepatitis B vaccine	24 (96)	23 (92)	22 (88)	21 (84)	20 (80)	19 (76)	19 (76)	19 (76)
Hepatitis A vaccine	24 (96)	23 (92)	22 (88)	21 (84)	20 (80)	19 (76)	19 (76)	19 (76)
Influenza virus vaccine	22 (88)	23 (92)	20 (80)	19 (76)	18 (72)	17 (68)	17 (68)	17 (68)
DTP or Td vaccine *	21/21 (100)	20/21 (95)	19/21 (90)	17/21 (81)	16/21 (76)	15/21 (71)	15/21 (71)	14/21 (67)

NSAIDs = non-steroidal anti-inflammatory drugs; MTX = methotrexate; IS = immunosuppressant (azathioprine, cyclophosphamide, cyclosporine or mycophenolate mofetil); TNF = tumor necrosis factor; BCG = bacillus Calmette-Guerin; MMR = measles, mumps and rubella; HPV = human papillomavirus; DPT = diphtheria, pertussis and tetanus.

* Four of 25 physicians interviewed reported that they vaccinated all patients up to 6 years of age with DPT, with rheumatic diseases and under any treatment, and patients older than 7 years with Td or DTaP (acellular triple bacterial).

Salk, Haemophilus and meningococcal C. All of them are composed of inactivated agents and therefore considered safe. These low rates of vaccination included patients at high risk of infection according to the same professionals. Possibly, this fact is explained by the remaining concern about the exacerbation or reactivation of disease, as recorded in JSLE patients following immunization against hepatitis B.⁷

Recently, pediatric rheumatologist members of the Department of Pediatric Rheumatology of SPSP met to establish consensus about immunization for patients with rheumatic diseases with onset in childhood and adolescence. At this point, a questionnaire was sent to all these renowned experts, which enabled this research. According to this consensus, it was concluded that there are few studies on efficacy and safety of using vaccines for these diseases in pediatric patients.⁸

According to the American Academy of Pediatrics, immunization with live vaccine component is contraindicated when prednisone is used in doses equal to or greater than 2 mg/kg or higher than 20 mg/day, for longer than a week.¹⁴ The Committee of Immunization Practices of the CDC instructs that live agents vaccines can be used in patients on MTX at doses ≤ 0.4 mg/kg/week or 28 mg/week in an individual

with 70 kg, azathioprine ≤ 3 mg/kg/day, or 6-mercaptopurine ≤ 1.5 mg/kg/day. The combination of these drugs with other immunosuppressant is not indicative of immunization.¹⁵

Davies & Woo found that, in the opinion of 24 rheumatologists from the British pediatric rheumatology group, the dose of CT that contraindicated the use of live attenuated virus vaccine (such as varicella vaccine) for children with rheumatic diseases was extremely varied.⁹ This effect was also observed among physicians specialized in pediatric rheumatology in the state of São Paulo participating in this study.

Over the years of follow-up and treatment with immunosuppressive drugs, surveillance of immunization with vaccination card was held by only 36% of the medical specialists. This study reinforces the need to include the item "vaccination" in the evolutionary medical record for all rheumatic diseases of childhood.

According to physicians, high risk of infection is associated with patients with JSLE and JDM. Immunosuppression of lupus is multifactorial and includes immunological changes characteristic of disease (dysfunction of phagocytes, lymphopenia, functional asplenia, reduced cytokines, immunoglobulins, and complement fractions), use of

Table 3
Practice of immunization with live and inactive agents according to time of practice

	Group A (n = 12)	Group B (n = 13)	P
Time of practice in pediatric rheumatology, median (range), years	10,5 (3-15)	24 (16-40)	< 0.0001
Recommended vaccines of live agents in general N (%)			
With NSAID	8 (67)	10 (77)	0.67
Without MTX, IS, or CT	9 (75)	9 (69)	1.0
MTX or single IS, without CT	1 (8)	0 (0)	0.48
Prednisone < 2 mg/kg/day, without MTX or IS	1 (8)	1 (8)	1.0
Prednisone < 2 mg/kg/day, with MTX or IS	2 (17)	0 (0)	0.22
Prednisone > 2 mg/kg/day, without MTX or IS	0 (0)	0 (0)	1.0
Prednisone > 2 mg/kg/day, with MTX or IS	0 (0)	0 (0)	1.0
With biological agents (anti-TNF, rituximab or abatacept)	0 (0)	0 (0)	1.0
Recommended vaccines of inactive agents in general N (%)			
With NSAID	12 (100)	12 (92)	1.0
Without MTX, IS, or CT	12 (100)	12 (92)	1.0
MTX or single IS, without CT	12 (100)	11 (85)	0.48
Prednisone < 2 mg/kg/day, without MTX or IS	11 (92)	11 (85)	1.0
Prednisone < 2 mg/kg/day, with MTX or IS	10 (83)	10 (77)	1.0
Prednisone > 2 mg/kg/day, without MTX or IS	9 (75)	10 (77)	1.0
Prednisone > 2 mg/kg/day, with MTX or IS	9 (75)	10 (77)	1.0
With biological agents (anti-TNF, rituximab or abatacept)	9 (75)	9 (69)	1.0

Group A (≤ 15 years of practice in pediatric rheumatology), Group B (≥ 16 years of practice in pediatric rheumatology). NSAIDs = nonsteroidal anti-inflammatory drugs; MT = methotrexate; IS = immunosuppressant (azathioprine, cyclophosphamide, cyclosporine or mycophenolate mofetil); TNF = tumor necrosis factor.

immunosuppressive, and disease activity.^{3,4} Infections also result in high mortality rates (between 9% and 30%) in patients with dermatomyositis.¹⁶ Lymphopenia, esophageal dysfunction, ventilatory insufficiency, interstitial lung disease, and calcinosis cutis are considered predictive parameters for infection in inflammatory myopathies.¹⁶

Some drugs commonly used for treatment of rheumatic diseases, such as CT, MTX, azathioprine, cyclosporine A, cyclophosphamide, and tumor necrosis factor inhibitors

(anti-TNF) are potentially immunosuppressive^{17,18} and were associated with high risk of infection by experts in this study. As expected, the use of NSAIDs and antimalarial drugs was considered low risk.

Some live virus vaccines are noteworthy. For children and adolescents with rheumatic diseases, the ideal would be to indicate the vaccine to children susceptible before starting immunosuppressive drug.¹⁵

Vaccines against varicella and yellow fever were contraindicated by all specialists in this study for patients receiving high-dose CT with or without the use of immunosuppressants. However, patients with rheumatic diseases present higher risk for severe varicella¹⁹ and herpes zoster,²⁰ in addition to additional risks related to chronic use of anti-inflammatory^{21,22} and possible induction of macrophage activation syndrome by this virus.²³

Despite concerns about the use of live agent vaccines, recent studies demonstrate the safety of its use in immunosuppressed patients. In a study conducted in Brazil, 25 pediatric patients with rheumatic diseases were selected and vaccinated against chickenpox. All patients were receiving MTX and 11 patients also received CT. No patient developed varicella and/or serious adverse events following vaccination. Moreover, no worsening in the activity of rheumatic diseases has been verified.²⁴ Another Brazilian study reported the practice of vaccination against yellow fever in seventy adult patients with rheumatic diseases, with mild adverse events observed in 22% of patients.²⁵

In conclusion, the practice of immunization surveillance by pediatric rheumatologists is low, especially after the first visit, possibly due to lack of efficacy and safety of vaccines in children and adolescents with rheumatic diseases. The frequency of indicating vaccines routinely is not influenced by the time of professional practice. Thus, the use of Consensus on Immunization for children and adolescents with rheumatic disease and regular checking of immunization cards, including teenagers, might improve the frequency vaccine recommendation in these patients. Furthermore, future multicentric trials including expressive populations of patients are needed.

REFERÊNCIAS

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1. Len CA, Terreri MT, Hilário MO. Lúpus eritematoso sistêmico juvenil e infecção. Rev Bras Reumatol 2002; 42(4):218-22.
2. Facó MM, Leone C, Campos LM, Febrônio MV, Marques HH, Silva CA. Risk factors associated with the death of patients hospitalized for juvenile systemic lupus erythematosus. Braz J Med Biol Res 2007; 40(7):993-1002.

3. Facó MM, Nukumizu LA, Pantoja AJ, Barros PC, Troster EJ, Silva CA. Avaliação dos óbitos e necropsias em pacientes internados em um Serviço de Reumatologia Pediátrica por um período de dez anos. *Rev Bras Reumatol* 2005; 45(2):55-63.
4. O'Neill SG, Isenberg DA. Immunizing patients with systemic lupus erythematosus: a review of effectiveness and safety. *Lupus* 2006; 15(11):778-83.
5. Gluck T, Muller-Ladner U. Vaccination in patients with chronic rheumatic or autoimmune diseases. *Clin Infect Dis* 2008; 46(9):1459-65.
6. Conti F, Rezai S, Valesini G. Vaccination and autoimmune rheumatic diseases. *Autoimmunity Reviews* 2008; 8(2):124-8.
7. Maillefert JF, Sibilia J, Toussirot E, Vignon E, Eschard JP, Lorcier B *et al.* Rheumatic disorders developed after hepatitis B vaccination. *Rheumatology (Oxford)* 1999; 38(10):978-83.
8. Silva CA, Terreri MT, Barbosa CM, Hilário MO, Pillegi GS, Ferriani VP *et al.* Consenso de imunização para crianças e adolescentes com doenças reumáticas. *Rev Bras Reumatol* 2009; 49(5):562-89.
9. Davies K, Woo P. Immunization in rheumatic diseases of childhood: an audit of the clinical practice of British Paediatric Rheumatology Group members and a review of the evidence. *Rheumatology (Oxford)* 2002; 41:937-41.
10. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997; 40(9):1725.
11. Petty RE, Southwood T, Manners P, Baum J, Glass DN, Goldenberg J *et al.* International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* 2004; 31(2):390-2.
12. Bohan A, Peter JB. Polymyositis and dermatomyositis. *N Engl J Med* 1975; 292(7):344.
13. Delbecq AL, Van de Ven AH, Gustafson DH (ed.). *Group Technique for Program Planning – a Guide to Nominal Group and Delphi processes.* Glenview, Illinois. Scott, Foresman and Company, 1975.
14. American Academy of Pediatrics. Committee of Infectious Diseases. Varicella-zoster infections circumstances. In: LK P (ed.) *r. Red Book.* 27 ed. Elk Grove Village, IL; 2005: p.672-86.
15. Cush JJ, Calabrese L, Kavanaugh A. Herpes zoster (shingles) vaccine guidelines for immunosuppressed patients. *American College of Rheumatology: Hotline* 2008; Aug 1.
16. Marie I. Infections in polymyositis and in dermatomyositis. *Presse Med* 2009; 38(2):303-16.
17. Snowden N. Immunisation of immunosuppressed patients with rheumatic diseases. www.arc.org.uk/arthritis/medpub/6632/6632.asp [cited 2007].
18. Luz KR, Souza DC, Ciconelli RM. Vacinação em pacientes imunossuprimidos e com doenças reumatológicas auto-imunes. *Rev Bras Reumatol* 2007; 47(2):106-13.
19. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde, Departamento de Vigilância e Epidemiologia, Programa Nacional de Imunizações. Manual dos Centros de Referência para Imunobiológicos Especiais (Cries). 2006. Disponível em: <http://www.cve.saude.sp.gov.br/>. Acesso em 20 de março de 2009.
20. Neves PS, Facó MM, Sallum AME, Campos LMA, Rossi Júnior A, Silva CA. Herpes zoster em pacientes com lúpus eritematoso sistêmico juvenil. *Rev Bras Reumatol* 2007; 47(2):135-9.
21. Bricks LF, Silva CA. Uso e abuso de anti-inflamatórios não hormonais: Parte I. *Pediatria (São Paulo)* 2005; 27(2):114-25.
22. Bricks LF, Silva CA. Toxicidade dos anti-inflamatórios não hormonais (AINH). *Pediatria (São Paulo)* 2005; 27(3):181-93.
23. Silva CA, Silva CH, Robazzi TC, Lotito AP, Mendroni Junior A, Jacob CM, *et al.* Macrophage activation syndrome associated with systemic juvenile idiopathic arthritis. *J Pediatr (Rio J)* 2004; 80(6):517-522.
24. Pileggi GC, Souza CBS, Ferriani, VPL. Safety and immunogenicity of varicella vaccine in patients with juvenile rheumatic diseases using methotrexate and glucocorticoids. *Arthritis Care Res (Hoboken)* 2010 (in press).
25. Mota LM, Oliveira AC, Lima RA, Santos-Neto LL, Tauil PL. Vaccination against yellow fever among patients on immunosuppressors with diagnoses of rheumatic diseases. *Rev Soc Bras Med Trop* 2009; 42(1):23-27.