Rheumatol Int (2014) 34:151–163
DOI 10.1007/s00296-013-2907-9

REVIEW ARTICLE

Comparison of national clinical practice guidelines and recommendations on vaccination of adult patients with autoimmune rheumatic diseases

Despoina Papadopoulou · Nikolaos V. Sipsas

Received: 1 September 2013 / Accepted: 15 November 2013 / Published online: 10 December 2013

Abstract The aim of the study is to identify and compare national recommendations on vaccination of adult patients with autoimmune rheumatic diseases (ARDs) in Europe, North America, and Australia. We conducted a search for recommended immunizations in adult patients with ARDs in the Medline database and the Web sites of National Rheumatologic Societies, Ministries of Health, National Advisory Committees on Immunization, and other relevant National Scientific Societies. We compared national guidelines and identified points of agreement and differences. Guidelines on vaccination of adult patients with ARDs were identified in 21 countries. Points of agreement include administering influenza and pneumococcal vaccines in addition to inactivated age-appropriate or travel-related vaccines, and avoiding the use of live vaccines in immunocompromised patients with ARDs. The most important differences concern the steroid dose that induces immunosuppression, the time interval between live vaccines and the initiation of immunosuppressive treatment, herpes zoster vaccination, and the preferred pneumococcal vaccine in patients with ARDs. We observed significant differences among national recommendations on immunizations in patients with ARDs, reflecting the lack of evidence-based data.

Keywords Autoimmune rheumatic disease · Vaccination · Recommendations

D. Papadopoulou (✉)
Pain and Palliative Care Clinic, Aretaieion Hospital and Medical School, National and Kapodistrian University of Athens, Vasilisis Sofias 76, 11528 Athens, Greece
e-mail: papadopould@med.uoa.gr

D. Papadopoulou
Rheumatology Outpatient Clinic, National Health Services, Peristeri, Athens, Greece

N. V. Sipsas
Infectious Disease Unit, Pathophysiology Department, Laikon General Hospital and Medical School, National and Kapodistrian University of Athens, Athens, Greece

Introduction

Infections are a major cause of morbidity and mortality in patients with autoimmune rheumatic diseases (ARDs). Factors contributing to the increased risk for infection include immune system dysfunction induced by the underlying disease, organ or mucosal injury (e.g., spleen infarcts, and skin ulcers), comorbidities, frequent hospitalizations, surgical procedures, and the use of immunosuppressive medications. Under-immunized patients with ARDs are vulnerable to serious infections, whereas inappropriate administration of vaccines in such patients can lead to serious adverse events [1–3]. Scientific societies in many countries have developed practice guidelines and/or recommendations aiming to provide guidance on the optimal use of vaccines and improve vaccination rates among patients with ARDs. The purpose of this review is to compare the existing recommendations in Europe, North America, and Australia.

Materials and methods

A Medline search was undertaken to identify immunization guidelines, recommendations, or consensus statements of National Societies for Rheumatology. Search terms included “society for rheumatology” OR “rheumatology association” OR “college of rheumatology” AND

"guidelines" OR "recommendations" OR "consensus." Of all articles retrieved, only those that included guidelines on immunization of adult patients with ARDs from Europe, North America, and Australia were included. An additional search in the references of retrieved systematic reviews was also performed.

Further search for guidelines/recommendations was conducted in the Web sites of national scientific societies, national health authorities, national committees on immunization practices (NCIP), professional organizations of rheumatologists, and organizations of rheumatologic patients. More specifically, we assessed the Web sites of the European National Societies for Rheumatology, the American College of Rheumatology, the Canadian Rheumatology Association, the Australian Rheumatology Association, the European League Against Rheumatism, and the International League Against Rheumatism. An additional search for Adult National Immunization Programs (NIPs) was performed in the Web sites of the European Center for Disease Control, the National Health Agencies of European countries, the Center for Disease Control and Prevention, the Public Health Agency of Canada, the Australian Department of Health and Ageing, and the World Health Organization. Links to Web pages of relevant scientific societies were followed.

There were no language or publication date restrictions. For articles written in languages other than English and French, electronic translators were used (http://translate.google.com/, http://www.bing.com/translator), either for primary translation or translation support.

Results

Countries with guidelines for the vaccination of patients with ARDs

We identified national recommendations on vaccination of adult patients with ARDs in 21 of the 55 countries included in our search (52 European countries, Canada, United States (US), and Australia). We also identified immunization guidelines developed by 17 National Societies for Rheumatology (Italy, Switzerland, Germany, Austria, Finland, United Kingdom, the Netherlands, Belgium, Spain, Portugal, Estonia, Czech Republic, France, Sweden, United States, Canada, and Australia) and 17 adult NCIPs (Italy, Greece, Denmark, Ireland, Slovenia, Czech Republic, Switzerland, Germany, Austria, Finland, United Kingdom, Spain, Belgium, France, United States, Canada, and Australia). The recommendations were made by working groups or panels and were based mainly on expert opinions, since clinical data are lacking.

Keeping immunization records

In eight countries (Switzerland [4], Germany [5–7], Finland [8], United Kingdom [9], Sweden [10], France [11–18], United States [19], and Canada [20, 21]), it is recommended to keep immunization record in all patients with the diagnosis of an ARD. More specifically, vaccination status should be checked during the initial workup of patients with ARDs, and catch-up vaccination for missed vaccine doses according to the general population program should be scheduled as soon as possible. Physicians should ensure that all vaccines indicated for patients with ARDs are kept up to date throughout the course of the disease.

Inactivated vaccines

A summary of recommendations for inactivated vaccines is provided in Table 1 [4–61].

Ideal timing for administering inactivated vaccines

Inactivated vaccines should ideally be administered prior to starting immunosuppressive treatment (12 countries) [4–8, 11–34]. Waiting at least 2 weeks before the initiation of immunomodulators is advised in six countries [8, 9, 14, 15, 20–23, 25–29, 33]. Alternatively, vaccinating during treatment breaks is suggested in three recommendations [22, 29, 31], with two [21, 29] recommending vaccination not earlier than 3 months after discontinuation of immunosuppressive drugs.

With regard to inactivated vaccines, if not previously administered or if booster vaccination is required, they can be given during treatment with DMARDs and biologics (16 countries) [5–7, 10–19, 21–27, 30–33, 35–41]. However, guidelines in eight countries [4, 5, 8, 10, 12, 13, 27, 30, 42, 43] include specific recommendations for rituximab (RTX), and all strongly recommend that inactivated vaccines should be administered before initiating RTX. In six countries, a specific interval of at least 4 weeks between vaccine administration and initiation of rituximab therapy is suggested. For patients already on rituximab, vaccination should be postponed for at least 2–6 months after the last infusion (Table 2) [4, 5, 8, 13, 27, 42, 43]. Additionally, three countries' guidelines recommend waiting 2 weeks before initiation of treatment with abatacept [5, 14, 30, 44]. Waiting 2 weeks before treatment with tocilizumab is recommended in the French guidelines [18]. Finally, vaccinating patients at a time when the disease is stable or when the dose of immunosuppressives is low is recommended in five guidelines [5, 10, 21, 22, 29].

Table 1 Recommendations on the administration of inactivated vaccines in Europe, North America, and Australia

Recommendation	Countries (ref)
Administration of inactivated vaccines prior to therapy initiation	Switzerland [4], Germany [5–7], Finland [8, 22, 23], Austria [24], United Kingdom [9, 25, 26], the Netherlands [27], Spain [28, 29], Czech Republic [30], France [11–18], United States [19, 31, 32], Canada [20, 21, 33], Australia [34]
Waiting to start treatment at least 2 weeks after inactivated vaccines	Finland [8, 22, 23], United Kingdom [9, 25, 26], the Netherlands [27], Spain [28, 29], France [14, 15], Canada [20, 21, 33]
Vaccination is best performed during treatment breaks	Finland [22], Spain [29] (at least 3 months after treatment cease), and Canada [21] (at least 3 months after treatment cease)
Inactivated vaccines can be given during immunosuppressive therapy	Italy [35], Greece [36], Switzerland [37], Germany [5–7], Austria [24], Finland [8, 22, 23], United Kingdom [9, 25, 26], the Netherlands [27], Spain [38], Estonia [39], Czech Republic [30], France [11–18], Sweden [10], United States [19, 31, 32], Canada [21, 33], Australia [40, 41]
Inactivated vaccines must be given prior to rituximab initiation	Switzerland [4], Germany [5, 42], Finland [8], United Kingdom [43], the Netherlands [27], Czech Republic [30], France [12, 13], Sweden [10]
Inactivated vaccines must be given prior to abatacept initiation	Germany [5, 44], Czech Republic [30], France [14]
Inactivated vaccines must be given prior to tocilizumab initiation	France [18]
Vaccines should be given when the disease is stable	Germany [5], Sweden [10], Finland [22]
Vaccines should be given when then dose of immunosuppressives is low	Germany [5], Spain [29], Canada [21]
Influenza vaccination	Italy [35, 45], Greece [36], Switzerland [4], Germany [5–7], Austria [24], Finland [8, 22, 23], United Kingdom [9, 25, 26, 43, 46], the Netherlands [27, 47], Belgium [48], Spain [28, 38], Czech Republic [30], France [11–18], Denmark [56], Ireland [57], Slovenia [58], Sweden [10], United States [19, 31, 32, 49], Canada [21, 33], Australia [40, 41, 50]
Pneumococcal vaccination	Italy [35, 45], Greece [36], Switzerland [4], Germany [5–7], Austria [24], Finland [8, 22, 23], United Kingdom [9, 25, 26, 43, 46], the Netherlands [27, 47], Belgium [48], Spain [28, 38], Czech Republic [30], France [11–18], Denmark [59], Ireland [60], Slovenia [61], Sweden [10], United States [19, 31, 32, 49], Canada [21, 33], Australia [40, 41, 50]
Meningococcal/*Hemophilus influenza* type b vaccine	*All immunocompromised patients:* Italy [53], Germany [5–7], Austria [24] *Asplenia and complement deficiencies:* Greece [36], Switzerland [37], Finland [8, 22, 23], United Kingdom [9], Spain [28, 29], France [12–18], Sweden [10], United States [32, 49], Canada [21], Australia [41]
Tetanus vaccination as recommended for the general population	Greece [36], Switzerland [4, 37], Germany [5–7], Austria [24, 51], Finland [8, 22, 23], United Kingdom [9], Spain [29], Czech Republic [30], France [11–18], Sweden [10], United States [31, 32, 49], Canada [21], Australia [41]
Hepatitis B vaccine	*High-risk patients and all patients with hand psoriasis*: Italy [35, 52, 53] *All patients before biologics*: Spain [28] *High-risk patients*: Greece [36], Germany [5, 6, 54], Austria [24, 51], Finland [22, 23], United Kingdom [46], the Netherlands [27], Czech Republic [30], France [12–18], Sweden [10], United States [19], Canada [33] *All immunocompromised patients*: Australia [41] Human papillomavirus vaccine Greece [36], Germany [5], France [11], Sweden [10], United States [19, 32, 49], Canada [20], Australia [41]
Typhoid vaccine	The Netherlands [47]
Q fever vaccine should be avoided	Australia [41]
Booster vaccination may be required	Switzerland [37], Germany [5], Austria [24], Finland [8, 22, 23], France [55], Canada [21], Australia [40, 41], United Kingdom [26, 46], United States [31]

Table 2 Existing guidelines on the ideal timing for administering inactivated vaccines to patients on rituximab

Country (ref)	Interval before rituximab (weeks)	Interval after rituximab (months)
Switzerland [4]	4	No recommendation
Germany [5, 42]	2–4	6
Finland [8]	4	No recommendation
United Kingdom [43]	4–6 (PPSV23)	No recommendation
The Netherlands [27]	4	2
France [13]	4	6

PPSV23 pneumococcal polysaccharide vaccine

Specific inactivated vaccines

Annual influenza vaccination is recommended in 19 countries [4–19, 21–28, 30–33, 35, 38, 40, 41, 47, 48, 50, 56–58]. In Australia, immunocompromised patients who receive influenza vaccine for the first time are recommended to receive 2 vaccine doses, at least 4 weeks apart and 1 dose annually thereafter. Additionally, in the setting of an influenza pandemic, it is advised to vaccinate immunocompromised persons with 2 doses of inactivated influenza vaccine, at least 4 weeks apart [41].

Pneumococcal vaccination is recommended in 19 countries [4–19, 21–28, 30–33, 35, 38, 40, 41, 43, 46–50, 59–62]. With regard to the type of pneumococcal vaccine, pneumococcal conjugate vaccine (PCV13) or pneumococcal polysaccharide vaccine (PPSV23), recommendations vary among different countries (Table 3) [4–11, 19, 20, 22–24, 27, 30, 36, 41, 50, 59–66]. More specifically, PCV13 is recommended in three countries, PPSV23 is recommended in seven countries, and various combinations of the two vaccines are recommended in nine countries.

Patients should be vaccinated with the tetanus–diphtheria–pertussis vaccine as recommended for the general population. This is mentioned specifically in the recommendations of 13 countries [4–18, 21–24, 29–37, 41, 49, 51]; however, in other countries, the general recommendation that "no precaution is needed as regards administering inactivated vaccines to immunocompromised patients," includes the Td(p) vaccine.

In the Netherlands, vaccinating patients with RA against typhoid fever vaccine is recommended [47].

Human papillomavirus (HPV) vaccination is generally recommended for patients with increased risk of persistent HPV infection and HPV-related disease, such as patients with systemic lupus erythematosus, but it may also be offered to all patients when adult catch-up vaccination is implemented in the NIP [5, 10, 11, 19, 20, 32, 36, 49]. The Australian Technical Advisory Group on Immunization (ATAGI) recommends HPV vaccine for immunocompromised adult patients regardless of age, even for men aged >26 and women aged >45 [41].

Meningococcal and *Hemophilus influenza* type b (Hib) vaccines are recommended for all patients with altered immune status only in Italy [53], Germany [5–7], and Austria [24], while in all other countries they are reserved for patients with asplenia or hypocomplementemia.

In twelve countries, hepatitis B virus (HBV) vaccination is not routinely recommended for patients with ARDs, but it is indicated if additional risk factors exist, especially before treatment with biologics [5, 6, 10, 12–19, 22–24, 27, 30, 33, 35, 36, 46, 51, 52, 54]. Routine vaccination of patients undergoing treatment with biologics if HBV serology markers are negative is recommended in Spain [28]. Vaccinating patients with chronic psoriatic lesions of the skin of the hands is recommended in Italy [53]. HBV vaccine is recommended in all eligible immunocompromised patients in Australia, due to the high possibility of severe disease [41].

Australian recommendations advise that the Q fever vaccine should be avoided in patients with altered immune status, as there are no data on the accuracy of skin testing or the efficacy and safety of Q fever vaccine in this population [41].

Booster doses

A special notice that the magnitude and duration of vaccine-induced immunity are often reduced in immunocompromised individuals is found in the recommendations of nine countries [5, 8, 21–24, 26, 31, 37, 40, 41, 46, 55]. In order to determine the need for booster doses, it might be useful to measure post-vaccination antibody titers. In the United States [31] and the United Kingdom [26, 46], all vaccine doses received while the patient is receiving immunosuppressive therapy or during the 2 weeks preceding therapy are not considered valid, and patients should be revaccinated with all vaccines that are still indicated at least 3 months after discontinuation of therapy.

Live vaccines

Vaccination with live vaccines is generally contraindicated during treatment with immunosuppressive agents, including high-dose steroids, DMARDs, and/or biologics.

Table 3 Guidelines on pneumococcal vaccination in patients with autoimmune rheumatic diseases and/or iatrogenic immunosuppression

Country (ref)	Recommendation
Italy [63]	PCV13 for pneumococcal vaccine-naïve patients aged >50, but also for patients aged <50 who are at risk for pneumococcal infection, such as patients with iatrogenic immunosuppression. If additional vaccination with PPSV23 is needed, it can be administered following a time interval >8 weeks For patients previously vaccinated with PPSV23, PCV13 can be administered at least 1 year after the last PPSV23 vaccination Severely immunocompromised patients can receive 2 doses of PCV13 at a distance >8 weeks
Switzerland [4]	PPSV23
Germany [5–7, 64]	Both PCV13 and PPSV23 should be used in patients with ARDs. Unvaccinated patients should first receive PCV13 followed by PPSV23 after 1 year. In patients previously vaccinated with PPSV23, PCV13 can be administered after 1–5 years
Greece [36]	PPSV23 for patients aged 19–49 PCV13 for patients aged >50
Austria [24]	PCV13 for adults >50 Adults >65 may receive either PCV13 or PPSV23 If sequential vaccination is required, the PCV13 and PPSV must have a minimum distance of 5 years between vaccinations
United States [19, 65]	*American College of Rheumatology:* PPSV23 *Centers for Disease Control:* Pneumococcal vaccine-naïve patients should receive a dose of PCV13 first, followed by a dose of PPSV23 at least 8 weeks later. A second PPSV23 dose is recommended 5 years after the first PPSV23 dose. Patients previously vaccinated with PPSV23 should be given PCV13 $\geq$ 1 year after the last PPSV23 dose
Finland [8, 22, 23]	PCV13 is the preferred vaccine Further protection with PPSV23 vaccine can be considered as early as 2 months after PCV13
Canada [20]	PPSV23
United Kingdom [9]	PPSV23
the Netherlands [27]	PPSV23
Belgium [67]	Primary vaccination with PCV13 followed by PPSV23 after 8 weeks Revaccination with PPSV23 after 5 years Patients previously vaccinated with PPSV23 can receive PCV13 after a period of more than 1 year
Spain [66]	PPSV23 for patients aged 19–49 PCV13 for patients aged >50. Additional PPSV23 vaccination after PCV13 can be considered Patients previously vaccinated with PPSV23 should be given a PCV13 dose $\geq$ 1 year after the last PPSV23 dose Severely immunocompromised patients can receive 2 PCV13 doses
Czech Republic [30, 62]	PPSV23
France [68]	Previously unvaccinated patients should receive PCV13 followed by PPSV23 after 8 weeks Patients previously vaccinated with PPSV23 should be given PCV13 after 3 years, followed by PPSV23 after 8 weeks
Sweden [10]	PPSV23
Denmark [59]	Previously unvaccinated patients should receive PCV13 followed by PPSV23 after 8 weeks Patients previously vaccinated with PPSV23 can receive PCV13 after a period of more than 1 year
Ireland [60]	PPSV23
Slovenia [61]	Either PCV13 or PPSV23
Australia [41, 50]	*Australian Rheumatology Association*: PPSV23 *Australian Technical Advisory group on Immunization*: Patients undergoing immunosuppressive treatment and asplenic patients should be given a dose of PCV13, followed by PPSV23 doses at a minimum of 2 months after PCV13. Adults previously vaccinated with PPSV23 should be given PCV13 at least 12 months after the most recent PPSV23 dose. A second PPSV23 dose is recommended at a minimum of 5 years after the first dose. A third dose is recommended at the age of 50 years for indigenous adults and 65 years for non-indigenous adults, or a minimum of 5 years after the second dose, whichever is later

PCV pneumococcal conjugate vaccine, *PPSV* pneumococcal polysaccharide vaccine

Live vaccines and steroids

The steroid dose that is considered to be sufficiently immunosuppressive to cause concerns for the safety of live vaccines is different among national guidelines (Table 4) [4, 5, 8, 9, 15, 20–23, 26, 29, 31, 37, 39, 40, 47, 61]. In most countries, live vaccines are contraindicated when a dose of >20 mg of prednisone or equivalent per day is administered systematically for >2 weeks [4, 5, 8, 20–23, 29, 31, 37]. In other national guidelines, the steroid dose

Table 4 Recommendations on the administration of live vaccines in patients receiving corticosteroids

Immunosuppressive daily dose of prednisone or equivalent (ref)	>20 mg for >2 weeks	>20 mg for >4 weeks	>10 mg for >2 weeks	>40 mg for >1 week	>60 mg for >1 week	Minimum time of steroid cease before live vaccines
Switzerland [4, 37]	✓					4 weeks
Germany [5]	✓					4 weeks
Finland [8, 22, 23]	✓					12 weeks
Spain [29]	✓					12 weeks
United States [31]	✓					4 weeks
Canada [20, 21]	✓					4 weeks
United Kingdom [9, 26]			✓	✓		12 weeks
Australia [40]					✓	4 weeks
France [15]			✓			No recommendation
Estonia [39]			✓			No recommendation
The Netherlands [47]			✓			2 weeks
Slovenia [61]		✓				No recommendation

that should restrain the use of live vaccines is >10 mg prednisone or equivalent per day administered systematically for >2 weeks [9, 15, 26, 39, 47]. An equivalent prednisone dose of >40 mg per day for >1 week is a contraindication for live vaccines in the United Kingdom [9]. In Australia, live-attenuated vaccines are contraindicated for adults receiving daily doses of oral corticosteroids in excess of 60 mg of prednisone (or equivalent) for more than 1 week [40]. If vaccination with a live vaccine is necessary, it should be postponed until at least two to twelve weeks after steroid treatment has been discontinued.

Live vaccines and DMARDs or/and biologics

The vaccination with live vaccines should be deferred for at least 3–6 months after discontinuation of DMARDs and 3–12 months after discontinuation of biologics. Treatment can be (re)-started 2–6 weeks after vaccination with a live vaccine. All information regarding specific drugs and variations among countries is included in Table 5 [4, 5, 8–10, 12–18, 20, 21, 24, 26, 29–31, 33, 35, 36, 39–41, 45, 47, 50, 51, 69, 70]. In Switzerland [4], Germany [5], the Netherlands [47], Czech Republic [71], France [11], and Australia [50], treatment with antimalarials and/or sulfasalazine is not a limitation for the administration of live vaccines. In Finland, a drug washout before vaccination with live vaccines is recommended for biologics but not for DMARDs. Moreover, the second dose of measles, mumps, and rubella vaccine, as well as varicella vaccine can be administered without previous biologic washout period [8].

Specific live vaccines

Varicella zoster virus (VZV) vaccine, indicated for use in adults over 60 years to prevent shingles, is recommended for selected patients with ARDs. The Advisory Committee on Immunization Practices (ACIP) [72], the ACR [19], the Canadian Immunization Guide [20, 21], and the Canadian Rheumatology Association [33] suggests that it may be administered to patients treated with short-term (<14 days) or low-to-moderate dose (<20 mg/day) corticosteroid therapy, leflunomide, sulfasalazine, low-dose methotrexate (≤0.4 mg/kg/week), or azathioprine (≤3.0 mg/kg/day) but it is not recommended for patients on biologics. According to the ATAGI [41], it may be appropriate to vaccinate with the zoster vaccine all patients anticipating immunosuppressive therapy, at least 1 month prior to the onset of immunosuppression; vaccination while receiving immunosuppressive therapy is not recommended.

Passive immunization

Intramuscular immune serum globulin can prevent or reduce the severity of disease if administered to susceptible individuals, such as patients with ARDs, within 6 days after exposure [73]. Passive immunization with the appropriate preparation of immunoglobulin (varicella zoster immunoglobulin or human normal immunoglobulin) after significant exposure to chickenpox, shingles, or measles should be considered in non-immune patients receiving immunosuppressive agents (Germany [6, 7], Austria [24, 51], United Kingdom [9, 74], Sweden [10], United States [75], Canada [76], Australia [41, 77]). Rituximab-treated patients with

Table 5 Recommendations for the administration of live vaccines in patients with ARDs receiving DMARDs and/or biologics

Country	Treatment discontinuation before live vaccines	Treatment (re)initiation after live vaccines
Switzerland [4]	3 months	4 weeks
Spain [29]	3 months	2 weeks
Germany [5]	3–6 months	
United States [31]	3 months	2 weeks
Finland [8]	No need to pause DMARDs 5 drug half lives for biologics Rituximab: until B cell count has returned to normal	4 weeks
United Kingdom [9, 26, 69]	3–6 months	4 weeks
Czech Republic [30, 71]	3 months for DMARDs 3 months for abatacept 6 months for rituximab 5 drug half-lives for other biologics	4 weeks
The Netherlands [47]	3 months for DMARDs 6 months for biologics	2 weeks (infliximab, etanercept, adalimumab, methotrexate, leflunomide) 4 weeks (rituximab, abatacept)
France [12–18]	Rituximab: 6 (if B cell count has returned to normal)-12 months abatacept: 3 months tocilizumab: 70 days Anti-TNF: 5 drug half-lives Methotrexate: 1–3 months	4 weeks
Canada [20, 21, 33]	3 months	2–4 weeks 6 weeks after varicella vaccination
Australia [40, 41, 50]	Not specified	4 weeks after zoster vaccination Not specified for other live vaccines
Italy [35, 45] Greece [36] Austria [24, 51] Portugal [70] Estonia [39] Sweden [10]	Not specified	Time not specified

TNF tumor necrosis factor, *MMR* measles, mumps, rubella, *DMARDs* disease modifying antirheumatic drugs

large and/or contaminated wounds should be given passive immunization with tetanus immunoglobulin (Sweden [10]). Human rabies immune globulin should be administered in previously unvaccinated immunocompromised patients with bites, scratches, or licks on broken skin/mucous membrane in a rabies-endemic area (Australia [41]). No specific recommendations regarding passive immunization of immunocompromized patients were identified in other countries.

Travelers with ARDs

Basic principles for administering travel-related vaccines to patients on immunosuppressive drugs are given in nine countries (Table 6) [5–8, 10, 12–18, 26, 27, 40, 41, 47, 78–80]. Patients should be vaccinated according to general recommendations, with the exception of live-attenuated vaccines that should be avoided. Travelers with severe immunosuppression should be strongly discouraged from traveling in yellow fever endemic areas. For patients who still wish travel to countries where yellow fever vaccination is mandatory, the general recommendations regarding treatment discontinuation before live vaccines and/or the time interval before treatment (re)initiation apply.

Household contacts of patients with ARDs

Recommendations regarding vaccination of household contacts are given in ten countries (Table 7) [5–7, 9, 18, 20–22, 24, 26, 31, 40, 41, 53, 55].

Discussion

We have identified agreements and differences regarding vaccination of adult patients with ARDs among national recommendations in Europe, North America, and Australia.

Points of agreement

Existing guidelines universally recommend vaccination for influenza and pneumococcal disease in patients with ARDs, based on the increased risk of pulmonary infections and

Table 6 Recommendations for vaccination of patients with ARDs traveling to endemic areas

Country (ref)	Travel vaccines guidelines
United Kingdom [26]	Inactivated poliomyelitis and typhoid vaccines should be used instead of OPV and the live typhoid vaccine in immunosuppressed patients YF vaccine is contraindicated Inactivated vaccines (e.g., rabies, anthrax, cholera, and plague) can be given
Germany [5–7]	The inactivated typhoid, the inactivated tick-borne encephalitis, and Hepatitis A vaccinations can proceed as usual Live vaccines (YF, oral typhoid, and cholera) are contraindicated during immunosuppressive treatment
United States [78]	Patients who are not being treated with immunosuppressive drugs or receiving therapy with < 20 mg of prednisone or equivalent, or if >1 month has passed since high-dose steroids have been used, should be prepared as any other traveler Patients taking high-dose corticosteroids or other immunosuppressive drugs should not be vaccinated with live travel vaccines (BCG, YF, oral typhoid) Inactivated travel vaccinations (typhoid, poliomyelitis, rabies, JE, HAV, HBV, and meningococcal) can proceed as usual
Sweden [10]	Patients should be vaccinated according to general recommendations, with the exception of live-attenuated vaccines (BCG, OPV, oral typhoid, and YF vaccines) that should be avoided
The Netherlands [27, 47]	For patients traveling in a less-developed area, vaccinations against HBV, rabies, and meningitis are recommended Traveling to areas where YF vaccine is mandatory is discouraged
Canada [79]	YF, oral typhoid, oral cholera, and BCG vaccines are contraindicated for patients receiving immunosuppressive treatment Inactivated typhoid, rabies, inactivated poliomyelitis, JE, HAV, HBV, meningococcal vaccinations can proceed as usual
France [12–18]	YF vaccine is contraindicated for patients receiving high-dose steroids and immunomodulators If YF immunization is mandatory, it should be administered at least 4 weeks before starting rituximab therapy, at least 3 weeks before starting abatacept, at least 2 weeks before starting tocilizumab and at least 3 weeks before TNFα antagonist or methotrexate initiation For patients already on treatment, YF vaccine is contraindicated within the first 12 months after rituximab therapy. Abatacept, tocilizumab, and TNF inhibitors should be stopped at least 5 times the drug half-life before administration of the vaccine. Methotrexate should be discontinued for 1–3 months if $CD4^+$ cells are <250/mm^3
Finland [8]	YF vaccine may be given 5 drug half-lives after the last treatment with biologics and at least 3 months after treatment with high-dose steroids has been paused
Australia [40, 41, 80]	Inactivated forms of poliomyelitis, JE, and typhoid vaccines must be used instead of OPV, live typhoid, and live JE vaccines in immunosuppressed travelers BCG and YF vaccines are contraindicated Intramuscular rabies vaccine, inactivated cholera, HAV, and other inactivated vaccines can be administered

YF yellow fever, *JE* Japanese encephalitis, *OPV* oral poliomyelitis vaccine, *BCG* Bacillus Calmette–Guérin, *HBV* hepatitis B virus, *TNF* tumor necrosis factor, *MMR* measles, mumps, rubella, *HAV* hepatitis A virus

evidence supporting efficacy and safety of these vaccines in ARD populations [81, 82]. Patients with asplenia or hypocomplementemia should additionally receive vaccination against *H. influenza* and *N. meningitidis* to provide optimal protection against encapsulated bacteria to which these individuals are highly susceptible [82, 83].Td boosters should be administered as scheduled for the general population regardless of immune status, since Td is not infectious and in patients with ARDs, it has demonstrated efficacy comparable to healthy controls [84]. HBV vaccination is efficacious in most patients with ARDs but the risk of hepatitis B in these patients is unknown [81]. Existing recommendations include HBV screening of patients with ARDs, in whom immunosuppression is being considered, and vaccination of non-immune patients at high risk for HBV infection [85, 86].

Regarding the ideal vaccination timing, there is consensus that administering inactivated vaccines prior to immunosuppressive therapy maximizes the immune response. Evidence linked to this recommendation is studies that showed an attenuated response to vaccination in recipients treated with immunosuppressive agents [87]. If, however, waiting to start treatment is not feasible, a general rule is that inactivated vaccines can be given safely to patients treated with immunomodulators. An important exception is treatment with rituximab. Several studies on the efficacy and safety of immunization in patients treated with B cell-depleting agents (i.e., rituximab) showed reduced response to influenza [88] and pneumococcal [89] vaccines; therefore, vaccines should be administered at least 4 weeks before RTX is started, or at least 6 months after therapy.

The administration of live vaccines in immunocompromised patients has been linked to substantial risk for infection due to the possibility of fatal reactivation of the

Table 7 Gudelines for the vaccination of household contacts of patients with ARDs receiving immunosuppressive agents

Country (ref)	Recommendation/precautions
Italy [53]	Annual influenza vaccination Varicella vaccination to unimmunized contacts
Germany [5–7]	Influenza (annually), pneumococcal, varicella, and MMR Contact with the patient should be avoided for 2 weeks following vaccination with oral typhoid, Rota virus vaccine, and OPV
Austria [24]	No limitation for administering any live (including varicella) vaccine to contacts of immunocompromised patients
United States [31]	All age-appropriate vaccines with the exception of smallpox vaccine and the live influenza vaccine Annual influenza Contacts can receive the varicella vaccine but if a rash develops after vaccination, direct contact should be avoided until the rash resolves Hand washing after changing the diaper of an infant who received rotavirus vaccine
Canada [20, 21]	Yearly influenza vaccination and up-to-date routine immunizations Varicella vaccine for non-immune contacts. If a post-vaccination rash develops, it should be covered and direct contact with the patient should be avoided for the duration of the rash MMR can be given if indicated
Finland [22]	Recommended vaccination: influenza (inactivated), MMR, Rota virus (infants)-special attention to hygiene for 2 weeks after vaccination, Varicella Not recommended: Live influenza, BCG, oral typhoid (contacts of severely immunocompromised), OPV
United Kingdom [9, 26]	Full immunization according to the United Kingdom schedule Additional vaccination against varicella and influenza MMR vaccine can be given if indicated OPV must not be given to contacts; the inactivated form can be used instead
Switzerland [37]	Unimmunized contacts must receive MMR and varicella vaccines
France [18, 55]	Varicella vaccination to unimmunized contacts. In case of rash, contact should be avoided for 10 days Influenza vaccination annually
Australia [40, 41]	All age-appropriate vaccinations MMR and varicella vaccine for non-immune contacts Annual influenza vaccination Herpes zoster vaccination for contacts aged ≥50 years. If a vaccinated contact develops a rash, it should be covered and contact with the patient should be avoided for the duration of the rash Hand washing after changing the diaper of an infant who received rotavirus vaccine

MMR measles, mumps, rubella, *OPV* oral poliomyelitis vaccine, *BCG*: Bacillus Calmette–Guérin

infectious agent contained in the vaccine [81]. Recommendations emphasize that live vaccines should not be used during immunosuppressive treatment, including high-dose steroids, DMARDS, and biologics.

Regarding travel guidelines, it is unknown whether the risk of travel-related infections is increased in ARD patients [81]. Before traveling to an endemic area, consultation with an infectious disease specialist should be sought. No limitations for inactivated travel-related vaccines were found. On the contrary, all travel-related live vaccines should be avoided in ARD patients treated with immunosuppressive drugs. These include BCG, oral poliomyelitis, oral typhoid fever, oral cholera, and yellow fever vaccines.

Differences among guidelines

Most differences concern the safe use of live vaccines in patients with ARDs, as there are no data regarding the required free of immunosuppressive therapy time for safe administration of these vaccines. A noteworthy exception is the Finish Society for Rheumatology recommendation that DMARD discontinuation is not necessary before vaccination with live vaccines. Moreover, the steroid dose that interferes with immune response and causes concerns for vaccine safety is different among guidelines as definitive studies are lacking.

Another notable discrepancy concerns the vaccine for varicella zoster virus (VZV). ARDs and their therapies may put patients at increased risk for shingles, but since this is a live-attenuated vaccine, caution is advised. NCIPs and rheumatology associations in Europe and Australia recommend avoiding VZV vaccination in patients receiving any immunosuppressive treatment since no studies have been performed in patients with ARDs. The European League Against Rheumatism (EULAR) task force on vaccination also recommends avoiding the use of any live-attenuated vaccine in immunosuppressed patients with ARDs; nevertheless, EULAR recommendations, recognizing the high burden of VZV in these patients, suggest that VZV vaccination may be an exception in selected,

mildly immunosuppressed patients [41, 81]. On the contrary, the ACR, ACIP, and the Canadian Rheumatology Association suggest that VZV vaccination in patients with ARDs should only be restricted during treatment with biologics and high-dose steroids. However, it should be emphasized that these recommendations are based on expert opinion [19–21, 33, 72]. Differences regarding the type of pneumococcal vaccine that patients with ARDs should receive were also found. These may be attributed to the delayed inclusion (2011) of the conjugate vaccine in the NIPs after receiving approval for the adult indication in the Europe [90] and the United States [91]. Moreover, data on PCV13 vaccination in patients with ARDs are still lacking [92].

Other differences include expanding vaccination coverage against *Haemophilus influenza* and *N. meningitidis* to all patients with ARDs (Germany, Austria, and Italy), and against HBV to all immunocompromised patients (Australia), all patients undergoing treatment with biologics (Spain) or patients with chronic psoriasis involving the skin of the hands (Italy). These differences are due to the lack of evidence on the safety and effectiveness of the relevant vaccines in patients with ARDs.

Our study has some limitations. Possible omission of recommendations cited elsewhere than Medline and National Health and Vaccination/National Rheumatology Societies official Web sites, or cited in Web pages, which require membership, or not retrieved due to deficient electronic translation of a Web page, must be acknowledged. Many NIPs and National Committees on Immunization make general recommendations for immunocompromised patients and do not give specific advice on patients with ARDs. Every effort was made to include solely recommendations for patients with ARDs and/or patients receiving steroids, DMARDs, and biologics.

In conclusion, vaccination national guidelines and/or recommendations in patients with ARDs have points of agreement but also several discrepancies. As evidence-based data are still limited, most recommendations are based on experts' opinion. Studies examining the effectiveness and safety of specific vaccines in patients with ARDs need to be conducted, as proper immunization is fundamental in this specific patient population. Future challenges include the harmonization of the existing guidelines and their implementation by integration into local care processes.

Acknowledgments NVS acknowledges support from the Special Account for Research Funds (ELKE) of the National and Kapodistrian University of Athens, Greece.

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

References

1. Rahier JF, Moutschen M, Van Gompel A et al (2010) Vaccinations in patients with immune-mediated inflammatory diseases. Rheumatology 49(10):1815–1827
2. Fessler BJ (2002) Infectious diseases in systemic lupus erythematosus: risk factors, management and prophylaxis. Best Pract Res Clin Rheumatol 16(2):281–291
3. Caporali R, Caprioli M, Bobbio-Pallavicini F, Montecucco C (2008) DMARDS and infections in rheumatoid arthritis. Autoimmun Rev 8(2):139–143
4. Swiss Society for Rheumatology (2010) Vaccination guidelines for patients with inflammatory rheumatic disease. Available from: http://www.rheuma-net.ch/download/Content_attachments/FileBaseDoc/recommandations-vaccination-04-2010.pdf (cited 2013 July 10)
5. Goldacker S, Gause A, Warnatz K (2012). German Society for Rheumatology Pharmacotherapy Commission quality assurance for vaccination in adult patients with inflammatory rheumatic diseases. Available from: http://dgrh.de/fileadmin/media/Praxis_Klinik/Therapie-Empfehlungen/impfung_qualitaetssicherung_final_2012.pdf (cited 2013 July 10)
6. Standing Committee on Vaccination (STIKO) at the Robert Koch Institute (RKI) (2012) Recommendations of the Standing Committee on Vaccination (STIKO) at the Robert Koch Institute. Epidemiol Bull 30:283–310. Available from: http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2012/Ausgaben/30_12.pdf?_blob=publicationFile (cited 2013 July 10)
7. Robert Koch Institute–German Federal Ministry of Health (2012) Vaccination recommendations by STIKO. Available from: http://www.rki.de/EN/Content/Prevention/Vaccination/recommandations/recommendations_node.html (cited 2013 July 10)
8. Repo H, Peltomaa R, Finnish Rheumatology Association (2012) Vaccination of adults with inflammatory rheumatic diseases. Available from: http://www.reumatologinenyhdistys.fi/files/rokotus.pdf (cited 2013 July 10)
9. Department of Public Health England (2013) Immunisation against infectious disease: the green book. Available from: http://immunisation.dh.gov.uk/gb-complete-current-edition/ (cited 2013 July 10)
10. Swedish Rheumatology Association (2011) SRF vaccination recommendations in patients with inflammatory rheumatic diseases. Available from: http://www.svenskreumatologi.se/sites/default/files/8/images/SRFs%20riktlinjer_vaccinationer_2011.pdf (cited 2013 July 10)
11. Dougados M (2010) Recommendations of the French Society for Rheumatology to detect or prevent diseases associated with chronic inflammatory rheumatism. Available from: http://www.rhumatologie.asso.fr/data/ModuleProgramme/PageSite/2010-1/Resume/6649.asp (cited 2013 July 10)
12. French Club of Rheumatism and Inflammation (2007) CRI factsheets. Available from: http://www.cri-net.com/recherche/fichesPratiques/ (cited 2013 July 10)
13. Pham T, Fautrel B, Gottenberg JE et al (2008) Rituximab (MabThera) therapy and safety management. Clinical tool guide. Joint Bone Spine 75(Suppl 1):S1–S99
14. Pham T, Bachelez H, Berthelot JM et al (2012) Abatacept therapy and safety management. Joint Bone Spine 79(Suppl 1):3–84
15. Pham T, Bachelez H, Berthelot JM et al (2011) TNF alpha antagonist therapy and safety monitoring. Joint Bone Spine 78(Suppl 1):15–185
16. Fautrel B, Pham T, Mouterde G et al (2007) Recommendations of the French Society for Rheumatology regarding TNFalpha

antagonist therapy in patients with rheumatoid arthritis. Joint Bone Spine 74(6):627–637
17. Pham T, Fautrel B, Dernis E et al (2007) Recommendations of the French Society for Rheumatology regarding TNFalpha antagonist therapy in patients with ankylosing spondylitis or psoriatic arthritis: 2007 update. Joint Bone Spine 74:638–646
18. Pham T, Claudepierre P, Constantin A et al (2010) Tocilizumab: therapy and safety management. Joint Bone Spine. 77(Suppl 1):S3–S100
19. Singh JA, Furst DE, Bharat A, et al (2012). 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 64(5):625–639
20. Public Health Agency of Canada (2012) Immunization and vaccines. Available from: http://www.phac-aspc.gc.ca/im/index-eng.php (cited 2013 July 10)
21. Public Health Agency of Canada (2007) Recommended Immunizations. Immunization of immunocompromized persons. Canadian immunization guide. Part 3. Available from: http://www.phac-aspc.gc.ca/publicat/cig-gci/p03-07-eng.php (cited 2013 July 10)
22. Finnish National Institute for Health and Welfare (2013) Vaccination of immunocompromized patients. Available from: http://www.thl.fi/fi_FI/web/rokottajankasikirja-fi/immuunipuutteiset (cited 2013 July 10)
23. Finnish National Institute for Health and Welfare (2013) Vaccination schedule. (http://www.thl.fi/fi_FI/web/fi/etusivu (cited 2013 July 10. Available from: http://www.ktl.fi/portal/suomi/terveyden_ammattilaisille/rokottaminen/ (cited 2013 July 10)
24. Austrian federal Ministry of health (2013) Austrian vaccination schedule 2013. Available from: http://bmg.gv.at/cms/home/attachments/3/3/6/CH1100/CMS1327680589121/impfplan2013.pdf (cited 2013 July 10)
25. The British Society for Rheumatology (2011) BSR statement on vaccination in adult patients with rheumatic diseases. Available from: http://www.rheumatology.org.uk/includes/documents/cm_docs/2011/b/bsr_vaccination_statement_nov_2011.pdf (cited 2013 July 10)
26. The British Society for Rheumatology (2002) Vaccinations in the immunocompromised person. Guidelines for the patient taking immunosuppressants, steroids and biologics therapies Available from: http://www.rheumatology.org.uk/resources/guidelines/archive_guidelines/default.aspx (cited 2013 July 21)
27. Dutch Society for Rheumatology (2011) Directive on responsible use of biologics. Available from: http://www.nvr.nl/uploads/Sk/A3/SkA3YYPbz5IMt3e8kt5fFg/Richtlijn_biologicals_geautorisateerde-versie_januari-2011.pdf (cited 2013 July 10)
28. Gómez Reino J, Loza E, Andreu JL et al (2011) Consensus statement of the Spanish Society of Rheumatology on risk management of biologic therapy in rheumatic patients. Reumatol Clin 7(5):284–298
29. Spanish Ministry of Health. Social Services and Equality (2004) Vaccination in adults-recommendations. Available from: http://www.msc.es/ciudadanos/proteccionSalud/vacunaciones/docs/recoVacunasAdultos.pdf (cited 2013 July 10)
30. Vencovský J, The Committee of the Czech Society for Rheumatology (2009) Safety recommendations on biological treatment. Čes Revmatol 17(3):146–160
31. National Center for Immunization and Respiratory Diseases (2011) General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 60(2):1–64
32. Centers for Disease Control and Prevention. (2013) Vaccination of persons with primary and secondary immune deficiencies. Available from: http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/A/immuno-table.pdf (cited 2013 July 10)
33. Bombardier C, Hazlewood GS, Akhavan P et al (2012) Canadian Rheumatology Association recommendations for the pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs: part II safety. J Rheumatol 39(8):1583–1602
34. Australian Rheumatology Association (2011) Updated recommendations for the use of biologic agents for the treatment of rheumatic diseases. Available from: http://www.rheumatology.org.au/downloads/FINAL-BiologicalRecommendations060111_000.pdf (cited 2013 July 10)
35. Italian Society for Rheumatology (2009) New influenza A (H1N1) advice of the Italian Society for Rheumatology for patients suffering from chronic inflammatory rheumatic diseases treated with immunosuppressive drugs and biological. Available from: http://www.reumatologia.it/cmsx.asp?IDPg=114#alto (cited 2013 July 10)
36. Greek National Organization of Health Services (2012) New national vaccination program of children and adolescents 2011 and adult immunization program. Available from: http://www.eopyy.gov.gr/Εγγραφα%20ΕΟΠΥΥ/Νέα%20-%20Ανακοινώσεις%20-%20Δελτία%20Τύπου/ΕΘΝΙΚΟ%20ΠΡΟΓΡΑΜΜΑ%20ΕΜΒΟΛΙΑΣΜΩΝ%20ΠΑΙΔΙΩΝ%20ΚΑΙ%20ΕΝΗΛΙΚΩΝ.pdf (cited 2013 July 10)
37. Swiss Federal Office of Public Health, Swiss Commission for Vaccinations (2013) Immunization: general recommendations. Swiss 2013 vaccinations plan. Available from: http://www.bag.admin.ch/themen/medizin/00682/00684/02535/index.html?lang=fr (cited 2013 July 10)
38. Spanish National Health System Library of clinical practice guidelines (2011) Update of the clinical practice guide for the management of rheumatoid arthritis in Spain. Available from: http://www.guiasalud.es/GPC/GPC_503_Guipcar_%28diciembre-2011%29.pdf (cited 2013 July 10)
39. Estonian Society for Rheumatology (2008) Rheumatoid arthritis-patient education material. (http://www.ers.ee/). Available from: http://www.ers.ee/index.php?id=112 (cited 2013 July 10)
40. Australian Government, Department of Health and Ageing (2013) Groups with special vaccination requirements. The Australian immunisation handbook, 10th edn. Chap 3.3. Available from: http://www.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10-3-3 (cited 2013 July 10)
41. Australian Government, Department of Health and Ageing (2013) Vaccine preventable diseases. The Australian immunisation handbook, 10th edn. Part 4. Available from: http://www.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10part4 (cited 2013 July 10)
42. Rubbert A, Burmester G, The Pharmacotherapy Commission of the German Society for Rheumatology (2007) Recommendations for the use of rituximab in patients with rheumatoid arthritis. Available from: http://dgrh.de/fileadmin/media/Praxis_Klinik/Therapie-Empfehlungen/rituximab_2013_final.pdf (cited 2013 July 10)
43. Bukhari M, Abernethy R, Deighton C et al (2011) BSR and BHPR guidelines on the use of rituximab in rheumatoid arthritis. Rheumatology (Oxford) 50(12):2311–2313
44. Krüger K, Gaubitz M, The Pharmacotherapy Commission of the German Society of Rheumatology (2008). Recommendations for the use of abatacept in patients with rheumatoid arthritis. Available from: http://dgrh.de/fileadmin/media/Praxis___Klinik/Therapie-Empfehlungen/abatacept_final.pdf (cited 2013 July 10)
45. Favalli EG, Caporali R, Sinigaglia L et al (2011) Recommendations for the use of biologic therapy in rheumatoid arthritis:

update from the Italian society for rheumatology II. Safety. Clin Exp Rheumatol 29(3 Suppl 66):S15–S27
46. Ding T, Ledingham J, Luqmani R et al (2010) BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies. Rheumatology (Oxford) 49(11):2217–2219
47. Dutch Society for Rheumatology. Gelre-IJssel Municipal Health Services (2008) Note on travel & vaccinations for patients on DMARDs & Biologics. Available from: http://www.nvr.nl/uploads/OK/pU/OKpULu4M6uy6R9GiuM9e4A/Notitie-reizen-en-vaccinaties.doc (cited 2013 July 10)
48. Belgian Royal Society for Rheumatology (2009) The Mexican Flu. Available from: http://www.srbr.be/fr/content/la-grippe-mexicaine (cited 2013 July 10)
49. Centers for Disease Control and Prevention (2013) Recommended adult immunization schedule. Available from: http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf (cited 2013 July 10)
50. Australian Rheumatology Association (2013) Patient information. Medicine information sheets. Available from: http://www.rheumatology.org.au/community/PatientMedicineInformation.asp (cited 2013 July 10)
51. Brezinschek H.P. and the Austrian Society for Rheumatology & Rehabilitation Working Group (2009) Opinion of the Austrian Society for Rheumatology on vaccination of patients with rheumatic diseases ('rheumatologic patients'). Available from: http://www.rheumatologie.at/pdf/OEGR-Stellungnahme_Impfen_16_Dez_2009.pdf (cited 2013 July 10)
52. Salvarani C, Pipitone N, Marchesoni A et al (2011) Recommendations for the use of biologic therapy in the treatment of psoriatic arthritis: update from the Italian Society for Rheumatology. Clin Exp Rheumatol 29(3 Suppl 66):S28–S41
53. Italian Ministry of Health (2012) Infectious disease and vaccination: national vaccine prevention plan. Available from: http://www.salute.gov.it/malattieInfettive/paginaInternaMalattieInfettive.jsp?menu=pianovaccini&id=651&lingua=italiano (cited 2013 July 10)
54. Manger B, Michels H, Nüsslein HG, et al (2006) Revision of the recommendations of the German society for rheumatology regarding therapy with tumor necrosis factor inhibitors in inflammatory rheumatic diseases. Available from: http://dgrh.de/fileadmin/media/Praxis___Klinik/Therapie-Empfehlungen/TNF-Blocker_06.pdf (cited 2013 July 10)
55. French Institute of Health (2010) The immunization schedule and vaccine recommendations in the opinion of the High Council of Public Health. BEH 14–15:121–172 Available from: www.invs.sante.fr/beh/2010/14_15/beh_14_15.pdf (cited 2013 July 10)
56. Statens Serum Institut- Danish Ministry of Health (2012) Free influenza vaccination. Available from: http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2039a%20-%202012.aspx (cited 2013 Aug 29)
57. Ireland Health Service Executive-National Immunisation Office (2013) Seasonal flu vaccine. Available from: http://www.immunisation.ie/en/AdultImmunisation/FluVaccination/ (cited 2013 Aug 29)
58. National Institute of Public Health- Republic of Slovenia (2013). Recommendations for vaccination of adults and children aged 5 years and older against pneumococcal infections. Available from: http://img.ivz.si/janez/2230-6991.doc (cited 2013 Aug 29)
59. Statens Serum Institut- Danish Ministry of Health (2012) Pneumococcal vaccination of persons at increased risk of invasive pneumococcal disease. Available from: http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2051b%20-%202012.aspx (cited 2013 Aug 29)
60. Ireland Health Service Executive-National Immunisation Office (2013) Pneumococcal. Available from: http://www.immunisation.ie/en/AdultImmunisation/Pneumococal/ (cited 2013 Aug 29)
61. National Institute of Public Health-Republic of Slovenia (2013) Vaccination against pneumococcal infection in adults and children. Available from: http://www.ivz.si/cepljenje/strokovna_javnost/navodila_in_priporocila?pi=18&_18_view=item&_18_newsid=2230&pl=253-18.0 (cited 2013 July 29)
62. Czech National Institute of Health (2011) The vaccination schedule in the Czech Republic. Available from: http://www.szu.cz/tema/vakciny/ockovaci-kalendar-v-cr?highlightWords=O%C4%8Dkovac%C3%AD+kalend%C3%A1%C5%99+%C4%8CR (cited 2013 Aug 29)
63. Italian Society of Hygiene (2013) Vaccination Board of the Italian Society of Hygiene indications of pneumococcal vaccine in adults at risk. Available from: http://www.igienistionline.it/docs/2012/30pneumo.pdf (cited 2013 July 29)
64. Mitteilung der Ständigen Impfkommission (STIKO) am Robert Koch-Institut (2012) Stellungnahme zur Impfung Erwachsener gegen Pneumokokken. Epidemiologisches Bulletin 7:55–62. Available from: http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2012/Ausgaben/07_12.pdf?__blob=publicationFile (cited 2013 July 10)
65. Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (2010) Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP): MMWR Morb Mortal Wkly Rep 59(34):1102–1106
66. Community of Madrid-Expert Vaccine Advisory Committee (2012) Pneumococcal vaccination for adults in the community of Madrid. Available from: http://www.madrid.org/cs/Satellite?c=PTSA_Multimedia_FA&cid=1142695928713&pagename=PortalSalud%2FPTSA_Multimedia_FA%2FPTSA_documentoWebeditpro (cited 2013 July 10)
67. Belgian Superior Health Board (2013). Vaccination of children and immunocompromised adults and chronically ill. Available from: http://www.cercles.be/base_cercle/fichiers_fiches/10536.pdf (cited 2013 July 29)
68. French High Council for Public Health (2013) Opinion on recommendations of vaccination for adults and children older than 2 years at risk of invasive pneumococcal disease. Available from: http://www.hcsp.fr/Explore.cgi/Telecharger?NomFichier=hcspa20130425_infectionsinvasivespneumocoque.pdf (cited 2013 Aug 29)
69. Chakravarty K, McDonald H, Pullar T et al (2008) BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. Rheumatology (Oxford) 47:924–925
70. Fonseca JE, Bernardes M, Canhão H et al (2011) Portuguese guidelines for the use of biological agents in rheumatoid arthritis—October 2011 update. Acta Reumatol Port 36:385–388
71. Šedová L, Štolfa J, Horák P, Pavelka K (2009) Czech Society for Rheumatology recommendations for monitoring the safety of the treatment of rheumatoid arthritis. Čes Revmatol 17(1):4–15
72. Harpaz R, Ortega-Sanchez IR, Seward JF, Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC) (2008) Prevention of Herpes Zoster. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 57(RR-5):1–30; quiz CE2-4
73. Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L (1998) Measles, mumps, and rubella vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 47(RR-8):1–57
74. Chakravarty K, Mcdonald H, Pullar T et al (2008) BSR/BHPR guideline for disease-modifying anti-rheumatic drug

(DMARD) therapy in consultation with the British Association of Dermatologists. Rheumatology (Oxford). doi:10.1093/rheumatology/kel216b
75. No authors listed (1993). Recommendations of the Advisory Committee on Immunization Practices (ACIP): use of vaccines and immune globulins in persons with altered immunocompetence. MMWR Recomm Rep 42(RR-4):1–18
76. Public Health Agency of Canada (2007) Passive Immunization. Canadian Immunization Guide. Part. Available from: http://www.phac-aspc.gc.ca/publicat/cig-gci/p05-01-eng.php (cited 2013 July 10)
77. Australian Government, Department of Health and Ageing (2013) Passive immunisation. The Australian immunisation handbook, 10th edn. Part 5 Available from: http://www.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10part5 (cited 2013 July 10)
78. Jong E, Freedman D (2012). Immunocompromised travelers. The yellow book. Chap 8. Centers for disease control and prevention. Available from: http://wwwnc.cdc.gov/travel/page/yellowbook-home-2012 (cited 2013 July 10)
79. Public Health Agency of Canada (2007) Recommended Immunizations. Immunization of travelers. Canadian Immunization Guide. Part 3. Available from: http://www.phac-aspc.gc.ca/publicat/cig-gci/p03-10-eng.php (cited 2013 July 10)
80. Australian Government, Department of Health and Ageing (2013) Vaccination for international travel. The Australian immunisation handbook, 10th edn. Chap 3.2 Available from: http://www.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10-3-2 (cited 2013 July 10)
81. van Assen S, Agmon-Levin N, Elkayam O et al (2011) EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 70(3):414–422
82. van Assen S, Elkayam O, Agmon-Levin N et al (2011) Vaccination in adult patients with auto-immune inflammatory rheumatic diseases: a systematic literature review for the European League Against Rheumatism evidence-based recommendations for vaccination in adult patients with auto-immune inflammatory rheumatic diseases. Autoimmun Rev 10(6):341–352
83. Styrt B (1990) Infection associated with asplenia: risks, mechanisms, and prevention. Am J Med 88(5N):33N–42N
84. Devey ME, Bleasdale K, Isenberg DA (1987) Antibody affinity and IgG subclass of responses to tetanus toxoid in patients with rheumatoid arthritis and systemic lupus erythematosus. Clin Exp Immunol 68(3):562–569
85. Kuruma KA, Borba EF, Lopes MH, de Carvalho JF, Bonfá E (2007) Safety and efficacy of hepatitis B vaccine in systemic lupus erythematosus. Lupus 16(5):350–354
86. Elkayam O, Yaron M, Caspi D (2002) Safety and efficacy of vaccination against hepatitis B in patients with rheumatoid arthritis. Ann Rheum Dis 61(7):623–625
87. Glück T, Müller-Ladner U (2008) Vaccination in patients with chronic rheumatic or autoimmune diseases. Clin Infect Dis 46(9):1459–1465
88. Oren S, Mandelboim M, Braun-Moscovici Y et al (2007) Vaccination against influenza in patients with rheumatoid arthritis: the effect of rituximab on the humoral response. Ann Rheum Dis 67(7):937–941
89. Bingham CO 3rd, Looney RJ, Deodhar A et al (2010) Immunization responses in rheumatoid arthritis patients treated with rituximab: results from a controlled clinical trial. Arthritis Rheum 62(1):64–74
90. European Medicines Agency (2011) Assessment report: Prevenar 13. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_Report_-_Variation/human/001104/WC500119784.pdf (cited 2013 July 29)
91. US Department of Health and Human Services. Food and Drug Administration Vaccines and Related Biological Products Advisory Committee (VRBPAC) (2011) Adult indication briefing document: Prevnar 13. Available from: http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/bloodvaccinesandotherbiologics/vaccinesandrelatedbiologicalproductsadvisorycommittee (cited 2013 July 29)
92. European Medicines Agency (2011). Prevenar 13. Summary of product characteristics. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001104/WC500057247.pdf (cited 2013 July 29)