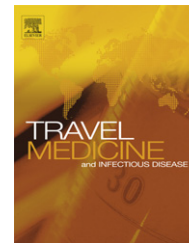




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## REVIEW

# Vaccination against tetanus, diphtheria, pertussis and poliomyelitis in adult travellers

Philippe Gautret <sup>a,\*</sup>, Annelies Wilder-Smith <sup>b</sup>

<sup>a</sup> *Service des Maladies Infectieuses et Tropicales, Hôpital Nord, AP-HM, Chemin des Bourrelys, 13915 Marseille cedex 20, France and Service de Pathologies Infectieuses et Tropicales, Hôpital d'Instruction des Armées Laveran, 4 Boulevard Alphonse Laveran, 13384 Marseille Cedex 13, France*

<sup>b</sup> *Travellers' Health and Vaccination Centre, Department of Medicine, National University Hospital, Yong Loo Lin School of Medicine, Singapore*

Received 13 July 2009; received in revised form 19 February 2010; accepted 23 February 2010  
Available online 19 March 2010

### KEYWORDS

Routine vaccinations;  
Childhood immunizations;  
Tetanus;  
Diphtheria;  
Poliomyelitis;  
Pertussis

**Summary** This paper reviews the risk and vaccine recommendations for tetanus, diphtheria, pertussis and poliomyelitis for adult travellers. The travel clinic presents a unique opportunity to evaluate whether routine vaccinations are up-to-date. Tetanus, diphtheria and pertussis occur worldwide but are more common in low resource countries due to incomplete childhood vaccination coverage, environmental and socio-economic factors. Diphtheria has been reported in travellers without adequate protection. A booster against tetanus and diphtheria is recommended for all adult travellers, regardless of travel destination and duration. The incidence of pertussis in general adult travellers has been poorly studied. Extrapolating from the reported high incidence in travellers to the Hajj, the risk may be more substantial than thought. There are no universal recommendations for pertussis vaccination for adult travellers, and studies are needed to develop evidence based guidelines. Poliomyelitis is well controlled and now only occurs in a small number of countries. Travellers to and from endemic and re-infected countries should be fully vaccinated against poliomyelitis.

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## Introduction

Immunizations in adolescents and adults provide challenges and opportunities.<sup>1</sup> Lack of awareness about the need for adult boosters, missed doses in childhood, neglected

vaccines for religious or other reasons, and the advent of new vaccines for catch-up vaccination require strategies for immunizations in adults. Travel clinics often serve as vaccination clinics thereby providing an ideal opportunity to offer routine vaccinations in addition to the classical

\* Corresponding author. Tel.: +33 4 91968934.  
E-mail address: [philippe.gautret@club-internet.fr](mailto:philippe.gautret@club-internet.fr) (P. Gautret).

travel related vaccines. Expert groups are unanimous in recommending updating of immunization against tetanus and diphtheria (Td) in all travellers and against poliomyelitis in travellers visiting an endemic country.<sup>2–4</sup> Despite these recommendations, vaccination coverage against Td, polio and pertussis was demonstrated to be low in travellers from numerous countries (Table 1) as evidenced in studies conducted in France,<sup>5–7</sup> Germany,<sup>8,9</sup> Australasia,<sup>10</sup> US,<sup>11</sup> South-Africa,<sup>12</sup> Spain<sup>13</sup> or Singapore.<sup>14</sup> We review the risk and vaccine recommendation for Td, poliomyelitis and pertussis for adult travellers.

## Tetanus and travel

Tetanus is ubiquitous, but has been largely eliminated in countries with effective immunization programs and good standards of hygiene but occurs occasionally in the elderly and other non- or insufficiently immunized people, as *Clostridium tetani* cannot be eliminated from the environment.<sup>15,16</sup> The disease is caused by a neurotoxin produced by anaerobic tetanus bacilli growing in contaminated wounds. Lesions that are considered “tetanus-prone” are wounds contaminated with dirt, feces or saliva, deep wounds, burns, crush injuries, or those with necrotic tissue.<sup>17</sup> However, tetanus has also been associated with apparently clean superficial wounds and insect bites.<sup>17</sup> Although there are no reports that travel itself is a risk factor for tetanus, injuries, insect and animal bites are not rare in returning travellers.<sup>18,19</sup> Tetanus is almost completely preventable by vaccination. Protection of travellers against tetanus is recommended to all travellers and is of particular interest in those performing high risk activities abroad exposing them to injuries and/or bites. The tetanus and diphtheria combined vaccine is recommended for primary immunization and booster doses in children >7 years and in adults. The diphtheria toxoid content in Td vaccine is lower, to decrease the likelihood of local side-effects at the site of injection. If the primary series has been completed but 10 years or more have elapsed since the last dose, a booster Td should be given. Any tetanus-prone wound should receive prompt local treatment by thorough cleansing and débridement of the wound if necrotic tissue or dirt is present.<sup>20</sup> Furthermore,

human tetanus immune globulin is indicated in travellers with tetanus-prone wounds who have an unknown or incomplete history of primary tetanus vaccination. Passive immunization consists of at least 250 IU of Human Tetanus immune globulin (TIG) intramuscularly, regardless of the patient’s age. When tetanus toxoid and TIG or antitoxin are given concurrently, separate sites must be used. Obtaining such post-exposure tetanus prophylaxis after minor or major injuries is time-consuming and disrupts travel plans as human tetanus immune globulin is not easily available in many developing countries. It is therefore imperative to take a history of prior tetanus vaccinations in every traveller and to update the tetanus immunization status combined with appropriate advice on wound management.

## Travel-associated diphtheria

Diphtheria is an acute bacterial disease caused by toxigenic strains of *Corynebacterium diphtheriae*. Humans are the only known reservoir of *C. diphtheriae*. Diphtheria is usually transmitted to close contacts by respiratory droplets or by direct contact with discharge from skin lesions. Diphtheria remains endemic in various developing countries in Africa, Latin America and Asia as well as in Albania, Russia and countries of the former Soviet Union<sup>16</sup> and several outbreaks occurred since 1990 (Table 2). The large diphtheria epidemic in the former Soviet Union 1990–1997 resulted in dozens of importations to Western Europe and North America and some travellers died while still in Russia.<sup>21</sup> Several travel associated respiratory diphtheria cases have been reported<sup>16,21–25</sup> and a fatal case occurred in a non-vaccinated traveller to Haiti, in 2003.<sup>26</sup> The far less serious form of cutaneous diphtheria is imported occasionally, mainly from developing countries,<sup>27,28</sup> even in correctly vaccinated individuals and may be responsible for secondary transmission in contacts. All travellers should be up-to-date with diphtheria toxoid vaccine before departure. As diphtheria toxoid is not manufactured as a monovalent vaccine, it is usually given in combination with tetanus toxoid or in combination with pertussis and/or poliomyelitis. The primary series in childhood consists of 5 doses. Thereafter, routine booster doses of reduced diphtheria toxoid vaccine should be given every 10 years, in

**Table 1** Vaccination coverage against tetanus, diphtheria, poliomyelitis and pertussis in travellers.

Place of study	Tetanus	Diphtheria	Poliomyelitis	Pertussis	Type of study
France	84%	—	68.7%	—	Airport survey (1994) <sup>5</sup>
Germany	70%	42%	49%	—	Airport survey (2001) <sup>8</sup>
Germany	73.3%	61.6%	66.3%	—	Airport survey (2001) <sup>9</sup>
South-Africa	59%	26%	46%	—	Airport survey (2003) <sup>12</sup>
Australasia	30%	14.5%	27%	—	Airport survey (2003) <sup>10</sup>
US	11%	7%	16%	—	Airport survey (2003) <sup>11</sup>
France	61%	—	—	—	Travel clinic survey (2002–2003) <sup>6</sup>
Spain	31.4%	31.4%	—	—	Airport survey (2004) <sup>13</sup>
France (Hajj pilgrims)	30%	25%	25%	13%	Travel clinic survey (2005) <sup>7</sup>
Singapore	33%	—	—	3%	Travel clinic survey (2006) <sup>14</sup>

**Table 2** Countries with outbreaks of diphtheria (since 1990) and confirmed wild poliovirus cases (2008–January–February 2009).

	Diphtheria <sup>16</sup>	Poliomyelitis <sup>38</sup>
Africa	Algeria, Sudan	Angola, Benin, Burkina Faso, Central African Republic, Chad, Côte d'Ivoire, Democratic Republic of Congo, Egypt, Ethiopia, Ghana, Kenya, Mali, Niger, Nigeria, Sudan, Togo, Uganda
Asia/South Pacific	Lao People's Republic, Mongolia, Papua New Guinea, Thailand	Afghanistan, India, Nepal, Pakistan
Middle East	Iraq	
Europe	Albania, Russia, and countries of the former Soviet Union	

adults. Diphtheria vaccination is especially important for travellers who will be living or working with local populations in countries where diphtheria is endemic. Patients with respiratory diphtheria require hospitalization, immediate treatment with diphtheria antitoxin, appropriate antibiotics and supportive care, and monitoring of their close contacts. Cutaneous diphtheria requires similar treatment but diagnosis is often difficult or delayed because the clinical appearance is nonspecific.<sup>27</sup>

### Travel associated pertussis

Pertussis is a worldwide, highly communicable, vaccine-preventable respiratory disease and is a frequent but often underestimated cause of prolonged cough in adults.<sup>29</sup> Immunity from childhood pertussis immunization is thought to last only up to 10 years.<sup>30,31</sup> The incidence of adult pertussis has been estimated to be 200–500 per 100,000 person-years.<sup>32–35</sup> Immunization against pertussis with acellular pertussis vaccine is recommended in adult risk groups such as health care workers as well as in adults with close contacts with children under 3 months. Data on the incidence of pertussis in the general adult travellers are lacking, and therefore it remains unknown whether travellers belong to a high risk group. One study found a high incidence of pertussis in a particular sub-population of travellers, namely the Hajj pilgrims.<sup>36</sup> The overall incidence of pertussis (1.4%) during this one month long pilgrimage was found to be higher than that of most other vaccine-preventable travel related diseases (with the exception of influenza) and higher than that reported in other risk groups such as health care workers. Hajj pilgrims would therefore benefit from pertussis vaccination prior to their departure. Given the fact that pertussis is a problem worldwide, pertussis is likely to be a risk to general travellers, compounded by the fact that national immunization programs against pertussis in some tropical destination countries may be suboptimal in infants. Furthermore, adult pertussis vaccine is actually not readily available in most developing countries and not therefore currently recommended even to those at high risk. Respiratory problems are the most common complaint in returning travellers as shown in a large cohort of more than 18,000 international travellers.<sup>19</sup> Travellers often encounter situations of overcrowding such as in airplanes, buses, trains, markets and festivals. Carefully designed studies to determine the

incidence of pertussis in general travellers are now needed to evaluate whether general travellers should be targeted for adult pertussis booster. Knowledge about pertussis was poor amongst adult travellers in a study done in Singapore. Although pertussis was viewed as a serious illness by the majority of participants, and 38% expressed the wish to be vaccinated, almost none had received a booster.<sup>14</sup> Awareness about pertussis, its risks and prevention by vaccination needs to be increased amongst adult travellers. Treatment of pertussis is based on antimicrobial therapy with a macrolide antibiotic, both to ameliorate the cough illness if given during the catarrhal stage or to limit transmission to others, once paroxysmal cough has developed. Prophylaxis is recommended for contacts.

### Travel associated poliomyelitis

Poliomyelitis is an acute viral infection that is acquired by fecal-oral or oral transmission. Poliomyelitis is close to eradication. The efforts of the Global Polio Eradication Initiative brought down the number of polio cases worldwide from 350,000 cases in more than 125 countries in 1988–2000 cases in nine countries in 2002. Only four countries (Afghanistan, India, Nigeria and Pakistan) have never completely interrupted transmission of wild polio virus (WPV).<sup>37</sup> However, a major obstacle to polio eradication appears to be international spread via travellers, be it refugees, pilgrims, traders or tourists. Between 2003 and 2006, polio was imported by travellers to 24 polio-free countries.<sup>37</sup> The origin of these importations was largely the 4 countries where polio transmission was never completely interrupted. The importations resulted in about 1400 secondary cases.<sup>37</sup> A total of 1655 WPV cases were reported worldwide during 2008, a 26% increase from 1315 cases reported in 2007.<sup>38</sup> Countries where WPV was reported in 2008-January-February 2009 are indicated in Table 2. Recently, poliomyelitis due to wild poliovirus was imported from Pakistan to a developed country, Australia, by an adult traveller who had visited friends and relatives in Pakistan. The individual had received oral polio vaccine during childhood but no booster dose before his travel.<sup>39</sup> This resulted in isolation of the case in hospital for 34 days. Household contacts were quarantined at home for 16 days. Together with potential contacts including airline passengers, health care workers and toilet contacts, 468 individuals were offered booster doses of IPV.<sup>40</sup>

Oral poliovirus vaccine (OPV) has been the vaccine of choice in most countries for successful mass immunization, as this vaccine suppresses intestinal excretion of poliovirus, is cheap and easy to administer. However, its disadvantage is the small but real risk of vaccine associated paralytic poliomyelitis (VAPP) in vaccinees and their contacts.<sup>41–44</sup> Inactivated poliovirus vaccine (IPV) has now replaced OPV in most developed countries as IPV is not associated with VAPP. However, OPV remains largely used in mass campaigns in developing countries. Cases of imported VAPP have been recently described in an unvaccinated US traveller to Costa-Rica where OPV is used<sup>45</sup> and suspected in a Canadian-born Chinese 6 month-boy following a trip to China.<sup>46</sup> Local transmission of imported OPV was demonstrated in an under-vaccinated Amish community in the US in relation with a case of VAPP in a child.<sup>47</sup> However, there is no serious risk of polio outbreak in populations where immunization coverage is high.<sup>48</sup> Sabin-like poliovirus have been recently isolated from wastewater in Switzerland where IPV is used reflecting the regular presence of virus-shedding individuals who return or enter from an OPV setting.<sup>49</sup>

To reduce the risk of international spread of polio via travellers, the Advisory Committee on Immunization Practices in 2006 proposed an additional strategy that would protect polio-free countries from re-introducing WPV by requiring proofs of vaccination against polio from all travellers from endemic countries traveling to polio-free countries.<sup>37</sup> The rationale is similar to that for yellow fever for which proof of vaccination is required for travellers as a condition of entry to certain countries. Saudi Arabia now requires that all travellers/pilgrims aged <15 years who are from polio-infected areas show proof of vaccination with oral polio vaccine 6 weeks prior to application for entry visa.<sup>50</sup> Such a requirement is not endorsed by the World Health Assembly, but is possible under the International Health Regulations.<sup>51,52</sup> Until the disease has been certified as eradicated globally, the risks of acquiring polio (for travellers to infected areas), and of re-infection of polio-free areas (by travellers from infected areas), remain. Travellers to and from endemic and re-infected countries should be fully protected by vaccination. Updates on countries with ongoing transmission of indigenous and imported WPV and countries with recent transmission of imported wild polio virus can be found at <http://www.polioeradication.org/casecount.asp>. Adults who are traveling to areas where poliomyelitis cases are still occurring and who are unvaccinated, incompletely vaccinated, or whose vaccination status is unknown should receive IPV (if available). Two doses of IPV should be administered at intervals of 4–8 weeks; a third dose should be administered 6–12 months after the second. If three doses of IPV cannot be administered within the recommended intervals before protection is needed, alternatives schedules may be used.<sup>53</sup> Adults with complete primary series who are traveling to areas where poliomyelitis cases are occurring and who have received a primary series with either IPV or OPV should receive only one other dose of IPV before departure.

Management of imported cases and prevention of ongoing transmission imply a rapid and extensive public health response as showed recently, in Australia.<sup>40</sup>

## Conclusion

Protection of travellers against tetanus is recommended for all travellers. Travel-associated diphtheria or poliomyelitis cases have been observed when traveling from developed countries to areas or countries with poor vaccine coverage. Updating immunization against these diseases should therefore not be neglected, particularly in elderly travellers whose vaccination coverage is often low.<sup>7,54</sup> However, many travellers do not have up-to-date vaccination certificates and cannot remember the date of their last booster. Determination of antibody level by enzyme-linked immunosorbent assay (ELISA) and sero-neutralization can be performed but is time-consuming and costly. A rapid dipstick test is available for the detection of protective tetanus immunoglobulin IgG antibodies and has been used successfully to identify travellers requiring a tetanus booster.<sup>55</sup> Clearly, rapid tests addressing the presence of protective antibodies against tetanus, diphtheria and poliomyelitis should be of great interest for travel medicine specialists. Studies are also needed to investigate the incidence of pertussis in travellers to provide evidence based guidelines about booster vaccination against pertussis in the travel medicine context. However, several national guidelines already recommend that adults should receive a single dose of tetanus, diphtheria and acellular pertussis vaccine to replace a single dose of tetanus and diphtheria for booster immunization and the travel clinic provides a unique opportunity for such booster doses and catch-up schedules.<sup>56</sup>

## Conflict of interest

PG was sponsored by GlaxoSmithKline and Sanofi-Pasteur to attend conferences. AW-S was sponsored by GlaxoSmithKline, Novartis and Sanofi-Pasteur to attend conferences, and has received speaking honoraria.

## Funding

None.

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