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## Travel medicine : knowledge, attitude, practice and immunisation

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### Citation

Roukens, A. H. E. (2010, March 4). *Travel medicine : knowledge, attitude, practice and immunisation*. Retrieved from <https://hdl.handle.net/1887/15037>

Version: Corrected Publisher's Version

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**Note:** To cite this publication please use the final published version (if applicable).

## **Health preparations and travel-related morbidity of kidney transplant recipients travelling to developing countries**

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*Clinical Transplantation 2007; 21:567-70*

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## Abstract

### **Background**

Improved health of solid organ transplant recipients has possibly led to increased travelling by this group. Since they are thought to be more susceptible to (travel-related) infectious diseases, as a result of their immunosuppressive medication, a survey was performed to investigate their travel profile and occurrence of travel-related diseases.

### **Methods**

A cross-sectional, descriptive study was conducted among Dutch kidney transplant recipients visiting the nephrology outpatient clinic. 290 completed a questionnaire (Q1). Of these, 103 travelled to (sub)tropical regions in the past 5 years. A mailed questionnaire (Q2) concerning occurrence and severity of travel-related diseases was returned by 71 individuals.

### **Results**

Thirty four percent of the respondents had travelled outside Western Europe (WE) and Northern America (NA); 22% of these travellers did not seek pre-travel health advice. Transplant physicians were most frequently consulted for pre-travel advice (53%). Of the respondents travelling outside WE and NA 29% were ill during their most recent journey. Four of seventeen ill recipients (24%) were hospitalised, reflecting the high morbidity of travel-related disease in this patient group.

### **Conclusion**

Our data show that there is need for improvement of pre-travel healthcare, and suggest an important role for transplant physicians in providing adequate counselling.

## Introduction

Modern surgical techniques and immunosuppressive therapy have greatly improved the health of solid organ transplant (SOT) recipients resulting in an increased mobility to different parts of the world, including tropical or subtropical destinations. Because of the continuous need for immunosuppression, SOT recipients are more susceptible to travel-related diseases and opportunistic pathogens than immunocompetent travellers [1,2]. A Canadian study revealed that SOT recipients are relatively unaware of these travel-related risks [3]. We investigated the travel health knowledge, attitude and practices of Dutch kidney transplant recipients (KTX) regarding preventive measures, adherence to these measures and consequences of illness while staying abroad, in order to assess the travel-related risks and to improve travel care in this patient group.

## Patients and methods

This cross-sectional, descriptive study was conducted at the nephrology outpatient clinic of the Leiden University Medical Centre (LUMC) in the Netherlands from December 2004 until January 2005.

A questionnaire (Q<sub>1</sub>) was distributed to all kidney and kidney-pancreas transplant recipients while waiting for their routine visit to their transplant physician. Patients participated on a voluntary basis. Q<sub>1</sub> focussed on demographics, on the medical history regarding organ transplantation, on information regarding travel of the past five years (destination, duration, purpose) and on pre-travel preparations.

Patients who had travelled outside Western Europe (WE) received a second, more extensive questionnaire (Q<sub>2</sub>) by mail. Q<sub>2</sub> assessed information on the most recent journey in the past five years (after transplantation) (destination, duration, purpose), on pretravel preparations, on medication taken during travel, on medical illnesses during travel and on its consequences.

To evaluate preventive measures and morbidity according to medical hazard, destinations were categorised into countries with (VAC<sup>+</sup>) and countries without (VAC<sup>-</sup>) recommendations for vaccination according to Dutch national travel guidelines [4]. VAC<sup>-</sup> countries are those in Western Europe, the Northern Americas, New Zealand and Australia.

Statistical analysis was performed using a computer-assisted software package (SPSS version 12.0). Student's *t*-test was used to compare continuous variables, the

Chi-square test for categorical variables. A 2-tailed p-value  $<0.05$  was considered statistically significant.

## Results

### Study population

A total of 290 of the approximately 400 individuals visiting the nephrology outpatient clinic completed Q<sub>1</sub>. Seventy-two recipients had their transplantation within the previous year. Six of the 72 recently transplanted SOT had travelled, of which 3 outside Western Europe (Curacao, Tunisia and Turkey). Since travelling is dissuaded during the first year after transplantation we excluded this patient group from further analysis (Figure 1).

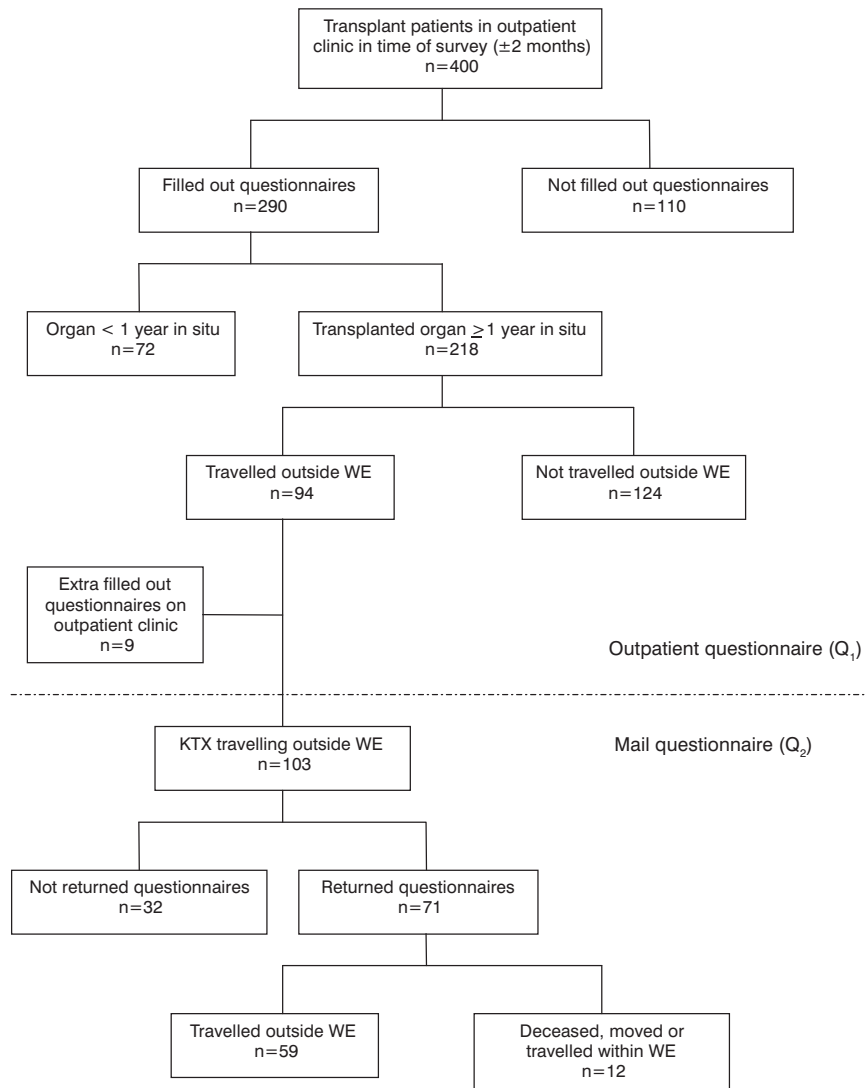
Q<sub>2</sub> was sent to 94 of the remaining 218 patients who had travelled outside WE, and to an additional 9 patients that had responded to Q<sub>1</sub> after the period of active recruitment (February 2005). Seventy-one of these 103 patients returned Q<sub>2</sub> (70% response rate). Twelve questionnaires were excluded (patients were deceased, had moved, or had their last travel within WE) leaving 59 questionnaires eligible for analysis.

Responders ( $N=59$ ) and non-respondents ( $N=32$ ) to Q<sub>2</sub> did not differ in terms of gender ( $p=0.5$ ), age ( $p=0.3$ ), transplant organ ( $p=0.4$ ) and post-transplantation period ( $p=0.9$ ). Demographic characteristics of the study population are listed in table 1. Nine of 59 respondents to Q<sub>2</sub> did not fill out their (immunosuppressive) medication. Usage of the following immunosuppressive medication was reported ( $N=50$ ): prednisone (95%), mycophenolate mofetil (47%), cyclosporine (42%), tacrolimus (27%), azathioprine (18%), mycophenolic acid (4%) and sirolimus (2%). Most KTX were on double (54%) or triple (42%) immunosuppressive therapy.

### Travel profile

The majority (80%) of the respondents to Q<sub>1</sub> reported to have travelled outside the Netherlands (NL), 43% travelled outside WE, and 34% outside WE and the northern Americas (NA) in the previous five years. No differences in gender, age, transplant organ or mean time since transplantation were observed between travelling and non-travelling respondents to Q<sub>1</sub>.

The mean duration of travel of the patients travelling outside WE (Q<sub>2</sub>,  $N=59$ ) was  $24.5 \pm 2.9$  (s.e.m.) days. Regions visited by the travellers outside WE (Q<sub>1</sub>,  $N=94$ ) were North America (23%), Africa (20%); North Africa, mostly Canary Islands (12%), and South Africa (8%), Eastern Europe (13%), Asia (12%) and Central America (11%),



**Figure 1** number of subjects enrolled in phase 1 (outpatient questionnaire,  $Q_1$ ) and phase 2 (mail questionnaire,  $Q_2$ ) of the survey.

**Table 1** Demographics of studied travelling kidney and kidney pancreas transplant recipients

|                                | Q <sub>1</sub> (n=218)       |       | Q <sub>2</sub> (n=59)        |       |
|--------------------------------|------------------------------|-------|------------------------------|-------|
|                                | % or mean<br>( $\pm$ s.e.m.) | range | % or mean<br>( $\pm$ s.e.m.) | range |
| gender (male)                  | 60                           | -     | 64                           | -     |
| age (yrs)                      | 50.5 $\pm$ 0.8               | 23-79 | 50.5 $\pm$ 1.7               | 24-78 |
| percentage kidney transplants  | 78                           | -     | 83                           | -     |
| transplant organ in situ (yrs) | 9.5 $\pm$ 0.5                | 1-37  | 9.5 $\pm$ 1.0                | 1-29  |

Q<sub>1</sub> is the outpatient questionnaire, Q<sub>2</sub> is the mail questionnaire which only the travellers outside Western Europe (N=103) received.

followed by the Caribbean (7%), Oceania (4%), South America (4%) and the Middle East (3%). In the Q2 population the major travel purpose was tourism (73%). Twenty four percent visited friends and relatives (VFR), and 3% travelled for business.

### Travel Health Preparations

Pre-travel health information was sought by 5% (Q<sub>1</sub>; 4 of 80) of responders travelling outside NL but within WE, 23% of travellers outside WE but within NA and 78% of travellers outside WE and NA ( $p < 0.01$ ). No statistical significant difference regarding gender, age, transplanted organ or time since transplantation was observed between respondents seeking pretravel advice and those not seeking advice (data not shown). Therefore, the data considering kidney and kidney pancreas transplant recipients were analysed as one group (KTX).

Travelling KTX who sought pre-travel advice (Q<sub>2</sub>, N=37) mostly consulted their transplant physician (53%), followed by a specialised travel clinic (16%) or their general practitioner (14%).

Regarding purpose of travel, travel health advice was sought by 28 of 42 (67%) tourists, and by 7 of 15 (46%) VFR. Responders to Q<sub>2</sub> and travelling to VAC<sup>+</sup> countries (N=25) more frequently sought pretravel advice (80%) than Q<sub>2</sub> respondents travelling to VAC<sup>-</sup> areas (N=34) (50%) ( $p = 0.03$ ).

### Accuracy of advice on vaccine-preventable diseases

Of the travellers seeking advice and travelling to VAC<sup>+</sup> regions, 15 respondents (79%) were vaccinated according to the national guidelines. The five unvaccinated individuals

travelled to Turkey ( $N=4$ ) or Colombia ( $N=1$ ). Four of these 5 obtained pretravel advice from their transplant physician.

### Travel related diseases

Seventeen respondents to Q<sub>2</sub> (29%; 95% CI 17-41) reported being ill during their most recent journey. Diarrhea was most frequently reported (44%; 95% CI 27-61, 14 of 32 reported symptoms), followed by fever (19%; 95% CI 5-33) and symptoms of respiratory tract infection (16%; 95% CI 3-29). Nine of 14 of travellers with diarrhea took additional medication (mainly antidiarrheal medication) of which only 2 reported to have taken antibiotics. No statistical difference was observed in the development of illness according to the number of immunosuppressants taken by respondents (data not shown).

Almost twice as many travellers visiting VAC<sup>+</sup> destinations (40%; 95% CI 21-59) reported symptoms of disease compared to those with VAC<sup>-</sup> countries (21%; 95% CI 7-35) however this difference did not reach statistical significance ( $p=0.1$ ). A significant difference was seen in illness in KTX travellers reporting to have taken oral diabetic medication (80%; 95% CI 45-100 ill) compared to non-diabetic travellers (24%; 95% CI 13-35 ill) ( $p=0.02$ ).

Consequences of illness for KTX during travel are listed in table 2. Four of the ill recipients (24%; 95% CI 4-48) were admitted to the hospital because of: syncope during a diarrheal episode ( $N=1$ ), *Salmonella* gastro-enteritis with transient renal failure ( $N=1$ ), ulcerative lesions in mouth and throat accompanied by diarrhea and weight loss ( $N=1$ ) and cellulitis of the lower limb ( $N=1$ ).

**Table 2** Type of medical care and absence from work due to travel-related disease in transplant recipients during travel outside Western Europe

|                                  | percentage of travellers<br>becoming ill ( $N=17$ ) | time (days)<br>(mean $\pm$ s.e.m.) | range<br>(days) |
|----------------------------------|-----------------------------------------------------|------------------------------------|-----------------|
| Use of additional medication     | 64                                                  | -                                  | -               |
| Contact physician on location    | 29                                                  | -                                  | -               |
| Contact physician in NL          | 29                                                  | -                                  | -               |
| Hospitalisation                  | 24                                                  | 25 $\pm$ 16                        | 1-56            |
| Absence from work due to illness | 29                                                  | 38 $\pm$ 16                        | 4-92            |

NL = the Netherlands.

## Discussion

In this survey, 75 of 218 respondents had visited a (sub)tropical destination in the past five years and tourism was the main reason for travelling. At least one in five immunocompromised travellers failed to obtain pre-travel health advice for these medically more hazardous destinations. In addition, there is room for improvement of the accuracy of advice on vaccine-preventable diseases. For example, 21% of travellers seeking information did not receive active or passive immunisation against hepatitis A while they should have, nor was immunoprotection confirmed by hepatitis A serology (data not shown). Furthermore, one third of the KTX travelling to VAC<sup>+</sup> and one fifth travelling to VAC<sup>-</sup> countries acquired a travel-related illness. Diabetic KTX travellers were most at risk. Finally, we found that almost a quarter of the ill travellers were hospitalised compared to less than 1% hospitalisation of ill, short term healthy travellers to the tropics [5].

Some potential limitations of this survey require comment: 1) we analysed travel behaviour of the last five years to reduce recall bias; 2) the number of kidney transplant recipients visiting friends and relatives (VFR) may be underestimated due to a language barrier resulting in failure to return the mailed questionnaire (Q<sub>2</sub>). In general, VFR are reported to be at greater risk of acquiring travel-related diseases [6].

Although very few studies have investigated practices, travel-related risks and complications experienced by solid organ transplant recipients travelling, the findings are surprisingly similar [3,7]. In the retrospective, descriptive study of mainly kidney and liver transplants recipients by Boggild et al. tropical destinations accounted for 48% of all travel; 34% travelling outside NA and WE failed to seek pre-travel advice, and in 78% the transplant physician was the source of information [3]. Of the travellers who became ill 56% had travelled to the tropics. In the retrospective, descriptive study of heart transplant recipients by Kofidis et al. travelling overseas was associated with a 45% complication rate in comparison to 22% for European destinations [7].

To conclude, we would like to make the following suggestions for improvement of travel care in this patient group. 1) transplant physicians have a central role in raising awareness of the risks and precautions for foreign travel after solid organ transplantation. A number of web links provide general information on risks and recommended preventive health measures [8]. For more specific advice referral to a specialised travel medicine centre is recommended. 2) As in non-compromised travellers, gastrointestinal and respiratory

tract infections were most frequently reported [9]. Diarrhea can lead to dehydration and may compromise renal function and increase toxicity of immunosuppressive medication [8]. Only 14% of respondents with diarrhea started self-treatment with antibiotics. Therefore, emphasis should be put on the importance of prompt self-treatment with antibiotics to reduce duration and severity of the diarrhea. 3) Finally, the need for prospective studies in this patient group remains.

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