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allergy testing due to a reported penicillin allergy. This represented approximately 5% of all cases managed at our institution over the time period. A beta-lactam-based regimen was considered the preferred treatment in all cases. The mean age of patients was 58 years (range 29–89), with 15 male patients and one female. Twelve patients had lesions consistent with endocarditis on echocardiography and 15 had positive microbiological samples (13 patients with positive blood cultures, one with organisms cultured from pacing wire tips and one with bacterial DNA detected in explanted valvular tissue by broad range 16s rDNA PCR). We estimated the time taken from diagnosis of endocarditis to allergy testing by using the date of the first diagnostic test or, in patients transferred to our centre with a diagnosis of endocarditis, date of admission. It took a mean of five days (range one to eleven). All patients tested negative for IgE-mediated allergy to penicillin on skin prick testing. Twelve patients also underwent oral drug provocation testing (flucloxacillin in seven, amoxicillin in four and co-amoxiclav in one). All but two patients had their antibiotics changed to the recommended first line (beta-lactam based) regimen following negative allergy testing; one patient had finished their antimicrobial course before undergoing allergy testing and complete antimicrobial records were unavailable for the other. Following introduction of beta-lactam therapy, only one patient developed an adverse reaction (rash). A summary of cases with aetiology and outcome is presented in Table 1.

The provision of allergy services in the UK is highly variable.⁷ Moreover, national guidelines for the management of drug allergy make no mention of the utility of inpatient testing in the management of selected patients with serious infections.⁸ We feel our experience strongly supports a role for inpatient allergy testing in patients with infective endocarditis; all of our tested patients likely benefited from a change to a more efficacious and less toxic antibiotic regimen. Such a service is also likely to be of benefit in the management of other infections requiring prolonged antibiotic courses, such as bone and joint and vascular graft infections.

Conflicts of interest

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Comparison of nasal swabs with throat swabs for the detection of respiratory viruses by real-time reverse transcriptase PCR in adult Hajj pilgrims



Dear Editor

Respiratory viruses, especially influenza viruses, are the main causes of acute respiratory infection in pilgrims during the Hajj.¹ Molecular methods are widely used for the rapid and accurate diagnosis of most common respiratory viruses.² Nasopharyngeal aspirates or nasal wash specimens are generally considered in clinical practice as the best specimens for respiratory viral diagnostics,³ but the use

of these invasive methods requires specialized training and equipment, making it inappropriate or unfeasible within the context of epidemiological field studies. Nose or throat swabs are useful tools for the rapid diagnosis of respiratory viruses using real-time reverse transcriptase-polymerase chain reaction (RT-PCR),⁴ especially within the context of Hajj studies, which are generally conducted among pilgrims as they arrive at and depart from the airport.^{5,6} We recently reported the nasal acquisition by French pilgrims of various respiratory viruses, including rhinovirus,^{7,8} and influenza viruses,⁹ by using RT-PCR. This study aims to compare nasal swabs with throat swabs for the detection of respiratory viruses in pilgrims by RT-PCR methods.

Individuals who are willing to participate in the 2013 Hajj were recruited at a travel agency in Marseille, France that is specialized in Hajj trips to Saudi Arabia. Paired nasal and throat swab specimens were systematically collected from all participants, whether symptomatic or not, by using commercial rigid cotton-tipped swab applicators, at two time points: 10 days before departing from France and one day before leaving Saudi Arabia, as previously described.⁸ All specimens were placed in viral transport media (Sigma Virocult[®]) at the time of collection and kept at 20 °C before being transported to a Marseille laboratory for storage in a -80 °C freezer within 48 h of collection. The protocol was approved by our institutional review board (July 23, 2013; reference no. 2013-A00961-44) and by the Saudi Ministry of Health Ethical Review Committee. All participants provided written informed consent.

Specimens were tested for the detection of various respiratory viruses (Table 1) by RT-PCR, as previously described.⁸ Total nucleic acids were purified from a 400 µL sample volume and were spiked with MS2+T4 bacteriophage as an internal control,¹⁰ using the BioRobot EZ1 XL with the Virus Mini kit v2.0 (both from Qiagen [Courtaubeuf, France]) according to the manufacturer's instructions. Each sample was tested independently in a 25 µL

reaction containing 5 µL of RNA, 12.5 µL of 2× buffer (iScript[™] One-Step RT-PCR Kit for Probes [Biorad]), 1 µL of reverse transcriptase/Taq, 400 nM concentration of each primer and 160 nM of probe. The reactions were performed using a C1000[™] Thermal cycler (CFX96[™] Real-Time System, BioRad, Marnes-la-Coquette, France). The following cycling conditions were applied: 50 °C for 10 min; followed by 95 °C for 5 min; and then 45 cycles of 95 °C for 15 s; and 60 °C for 30 s. The presence of inhibitors was determined using MS2 and T4 bacteriophage specific detection systems, as previously reported.¹⁰

Statistical analyses were performed using SPSS software version 17 (SPSS Inc., Chicago, IL, USA). Pearson's Chi-square test and Fisher's exact test, as appropriate, were applied to analyze categorical variables. The PCR results from paired nasal and throat swab specimens were compared using McNemar's test. *P* values of 0.05 or less were considered significant.

In total, 129 participants were enrolled in the study. There were 77 females (59.7%) and 52 males (40.3%) with a mean age of 61.7 years (SD, 9.8; age range, 34–85). About half of the participants (52.7%) declared suffering from at least one chronic disease, as described elsewhere.⁹ During the three-week stay in Saudi Arabia, most of pilgrims (90.7%) suffered from at least one respiratory symptom, including cough (86.8%), sore throat (82.9%), rhinorrhoea (72.1%), myalgia (50.4%), and feverishness (49.6%), and 47.3% met the criteria for self-reported ILI (defined according to the presence of the triad of a cough, sore throat, and subjective fever), as previously reported.⁸

A total of 250 paired nasal and throat swab specimens were collected (500 specimens), of which 121 were collected before departing from France and 129 were collected before leaving Saudi Arabia. Of the 250 paired specimens, 92 (36.8%) tested positive for at least one respiratory virus in one or both swabs, 36 (14.4%) were positive for at least one respiratory virus in the nasal swabs

Table 1 Prevalence of respiratory viruses in nasal and throat swab specimens collected from the study participants.

Respiratory virus	No. (%) of positive specimen			<i>P</i> value ^a
	Either swabs	Nasal swab	Throat swab	
Influenza virus A/H3N2	8 (3.2)	8 (3.2)	3 (1.2)	0.06
Influenza virus B	1 (0.4)	1 (0.4)	0 (0.0)	1
Influenza virus C	2 (0.8)	2 (0.8)	0 (0.0)	0.50
Influenza virus 2009 A(H1N1)	1 (0.4)	1 (0.4)	0 (0.0)	1
Human adenovirus	6 (2.4)	2 (0.8)	5 (2.0)	0.37
Human bocavirus	2 (0.8)	2 (0.8)	0 (0.0)	0.50
Human coronaviruses ^b	27 (10.8)	25 (10.0)	20 (8.0)	0.18
Human cytomegalovirus	0 (0.0)	0 (0.0)	0 (0.0)	—
Human enterovirus	8 (3.2)	4 (1.6)	5 (2.0)	1
Human metapneumovirus	3 (1.2)	3 (1.2)	0 (0.0)	0.25
Human parainfluenza viruses	5 (2.0)	5 (2.0)	4 (1.6)	1
Human parechovirus	1 (0.4)	0 (0.0)	1 (0.4)	1
Human respiratory syncytial virus	1 (0.4)	1 (0.4)	0 (0.0)	1
Human rhinovirus	48 (19.2)	36 (14.4)	24 (9.6)	0.07
At least one virus	92 (36.8)	76 (30.4)	56 (22.4)	0.008

^a McNemar's test (nasal swab versus throat swab).

^b Other than Middle East respiratory syndrome coronavirus

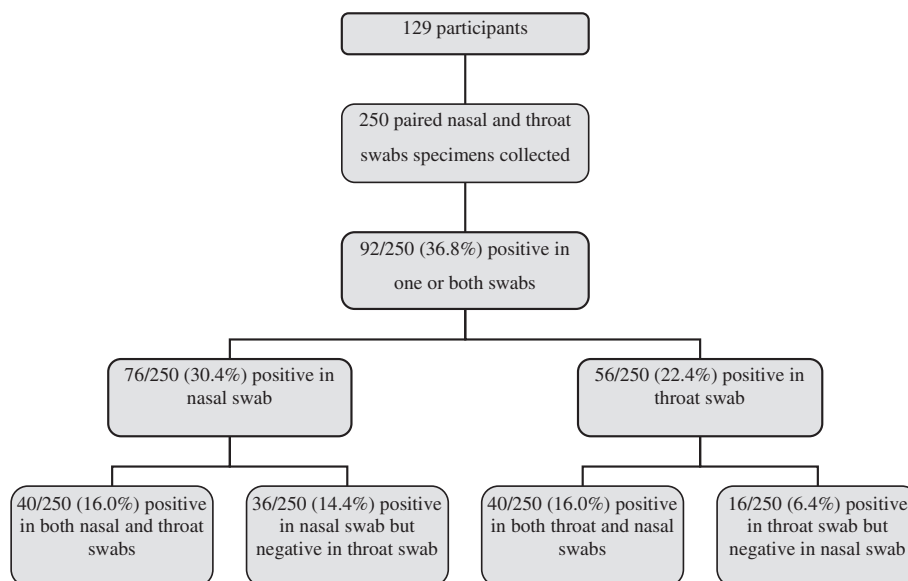


Figure 1 Prevalence of at least one respiratory virus in paired nasal and throat swab specimens collected from the study participants.

but negative in the throat swabs, 16 (6.4%) were negative for at least one respiratory virus in the nasal swabs but positive in the throat swabs, and 40 (16.0%) tested positive for at least one respiratory virus in both the nasal and throat swabs (Fig. 1). At least one respiratory virus was detected in 76 (30.4%) of a total 250 nasal swab specimens and in 56 (22.4%) of a total 250 corresponding throat swab specimens (McNemar's, $P = 0.008$) (Table 1). A subgroup analysis according to the presence of respiratory symptoms at the time of sampling also showed superior performance for nasal swabs compared to throat swabs (data not shown). Overall influenza viruses were detected in 12 nasal swabs (4.8%) and 3 (1.2%) throat swabs (McNemar's, $P = 0.004$). For most of the other viruses, there was a trend toward greater viral detection rates for the nasal swab specimens as compared to throat swab specimens, although the differences were not statistically significant (Table 1). However, the nasal swab failed to detect rhinovirus in 12 (25.0%) cases, adenovirus in 4 cases (50.0%), enterovirus in 4 cases (66.6%), and coronaviruses (other than Middle East respiratory syndrome coronavirus) in 2 (7.4%) cases. Overall, the addition of throat swab specimens allowed the detection of 23 (20.4%) additional viruses and the identification of 16 (6.4%) more infected individuals.

In conclusion, nasal sampling appeared to be significantly more effective than throat sampling in detecting respiratory viruses, notably influenza viruses, in adult pilgrims using RT-PCR methods. The combination of nasal and throat swabs increases the likelihood of detecting most viruses and represents an alternative to nasopharyngeal aspirate or nasopharyngeal swabs that are difficult to implement within the context of Hajj epidemiological studies.

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Conflicts of interest

The authors declare no conflicts of interest.

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