Incidence, Etiology, and Symptomatology of Upper Respiratory Illness in Elite Athletes

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ABSTRACT

SPENCE, L., W. J. BROWN, D. B. PYNE, M. D. NISSEN, T. P. SLOOTS, J. G. MCCORMACK, A. S. LOCKE, and P. A. FRICKER. Incidence, Etiology, and Symptomatology of Upper Respiratory Illness in Elite Athletes. *Med. Sci. Sports Exerc*., Vol. 39, No. 4, pp. 577–586, 2007. **Purpose:** Upper respiratory illness (URI) is the most common medical condition affecting elite athletes. The aims of this study were to identify and evaluate the incidence, pathogenic etiology, and symptomatology of acute URI during a 5-month training and competition period. **Methods:** Thirty-two elite and 31 recreationally competitive triathletes and cyclists, and 20 sedentary controls (age range 18.0–34.1 yr) participated in a prospective surveillance study. Nasopharyngeal and throat swabs were collected from subjects presenting with two or more defined upper respiratory symptoms. Swabs were analyzed using microscopy, culture, and PCR testing for typical and atypical respiratory pathogens. The Wisconsin Upper Respiratory Symptom Survey (WURSS-44) was used to assess symptomatology and functional impairment. **Results:** Thirty-seven URI episodes were reported in 28 subjects. Incidence rate ratios for illness were higher in both the control subjects (1.93, 95% CI: 0.72–5.18) and elite athletes (4.50, 1.91–10.59) than in the recreationally competitive athletes. Infectious agents were identified in only 11 (two control, three recreationally competitive, and six elite) out of 37 illness episodes. Rhinovirus was the most common respiratory pathogen isolated. Symptom and functional impairment severity scores were higher in subjects with an infectious pathogen episode, particularly on illness days 3–4. **Conclusion:** The results confirm a higher rate of URI among elite athletes than recreationally competitive athletes during this training and competition season. However, because pathogens were isolated in fewer than 30% of URI cases, further study is required to uncover the causes of unidentified but symptomatic URI in athletes. Despite the common perception that all URI are infections, physicians should consider both infectious and noninfectious causes when athletes present with symptoms.
Key Words: EXERCISE, INFECTION, IMMUNE, COMMON COLD, VIRAL, BACTERIAL

Evidence from several cross-sectional and prospective studies suggests that many elite and highly trained athletes experience more common colds or upper respiratory tract infections (URTI) than recreational athletes (9,13,14). Many studies have shown an association between decreased immune function and augmented exercise workloads, purportedly increasing the susceptibility to URTI (5–7,18,25,26). Acute URTI is the most common reason for presenting to a sports medicine clinic (11,20), and it is the most common medical condition affecting athletes at both the summer and winter Olympic Games (13,29). For example, data from the Sydney 2000 Olympic Games show that 33% of all consultations with the New Zealand medical team were categorized as respiratory tract illnesses (excluding asthma) (30). Anecdotally, there are many examples of elite athletes being unable to compete in high-level international competition

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because of URTI. There is, therefore, a clear need for better understanding of the etiology of URTI in elite athletes and of the diagnostic and treatment difficulties faced by physicians who deal with athletes presenting with upper respiratory symptoms during periods of intensive training and competition.

Although there has been substantial research in the field of exercise immunology and infection during the last two decades, the actual pathogenic *causes* of upper respiratory disturbances in athletes have not been clearly elucidated. None of the previous human epidemiological studies showing that intense exercise increases the risk of URTI (and that moderate exercise is associated with reduced risk) have comprehensively determined the etiology of the infections described (22,23,28). Since the 1950s, research has been undertaken in general populations to identify the etiology of URTI (more commonly known as the common cold). Overall, this research has provided evidence that viruses including rhinovirus, adenovirus, and parainfluenza virus are the primary causes of these symptoms (17) and that bacterial infections are infrequent, particularly in uncomplicated cases. Most of these studies have noted that 30–40% of illness episodes do not have an identifiable pathogen associated with them.

Other studies undertaken in elite athletes have focused on the relationship between immunosuppression and risk, susceptibility, or incidence of URTI. However, because the microbes and processes that cause upper respiratory disturbances in athletes have not been identified, it is not known whether changes in the immune system of elite athletes result from a specific microorganism (e.g., Epstein–Barr virus, or EBV (4,12)), or an as-yet unknown mechanism or mediator. To date, most of the infection data in training studies have been based on self-reported illness logs, and none have been validated with objective measures of infection (8,16,25–27,33). There is, therefore, a clear need for well-controlled prospective studies involving objective laboratory assessment of causes and symptoms of illness in elite athletes, to facilitate accurate diagnosis, treatment, and management by physicians.

The aims of this study were to determine the incidence, pathogenic etiology, and symptomatology of acute upper respiratory illness (URI) in sedentary, moderately active, and highly trained athletes during a 5-month training and competition period.

METHODS

Subjects and study design

This prospective surveillance study was conducted from December to April during the southern hemisphere's summer and autumn months in the temperate climate of southeast Queensland, Australia. During this time, mean daily maximum temperatures range from 30.4°C in January to 26.2°C in April (yearly average 26.2°C), and mean monthly rainfall ranges from 244.0 mm in February to 80.8 mm in March (yearly average 71.6 mm per month; Australian Government, Bureau of Meteorology data). In southeast Queensland, acute respiratory tract infections peak in winter (31).

Thirty-two elite male and female triathletes and cyclists (age 18–34 yr) from the Australian Institute of Sport and Queensland Academy of Sport squads based in southeast Queensland, 31 male and female recreationally competitive triathletes and cyclists (age 19–34 yr) from local training clubs, and 20 male and female untrained sedentary controls (age 19–29 yr) from university and laboratory staff, were recruited into the 5-month prospective surveillance study. The subjects were selected as untrained sedentary controls if they were undertaking less than 60 $min \cdot wk^{-1}$ of moderate-intensity ($\geq$ 3.0 metabolic equivalents, or METs) exercise during the baseline assessment period and if they were not planning to change their exercise or activity levels for the duration of the study.

After an initial information session, during which the procedures, benefits, and potential risks of the study were described, each subject gave written informed consent and completed a comprehensive health and medical questionnaire. Both athletes and controls were in good health, not using medications known to affect immune function or inflammation, and did not smoke cigarettes or consume large amounts of alcohol. The subjects reported they had been free of illness symptoms for the 2 wk preceding the baseline measures. This study was approved by the medical research ethics committee at the University of Queensland and the Australian Institute of Sport ethics committee. All procedures conformed to the National Health and Medical Research Council guidelines for experimentation with human subjects and were performed in accordance with the Helsinki Declaration.

The timeline for the 5-month prospective surveillance study is shown in Figure 1. Before baseline assessment, the elite triathletes and cyclists were maintaining low-volume,

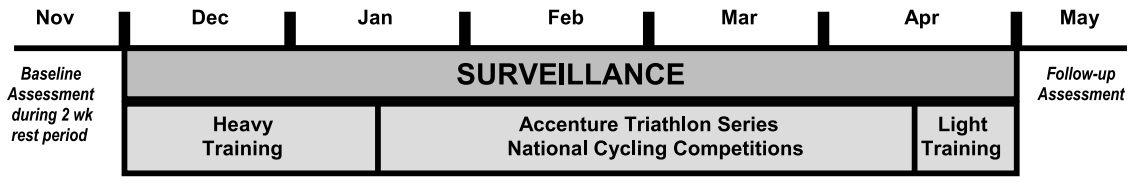

FIGURE 1—Timeline for the 5-month surveillance study.

moderate-intensity training after the main national and international competitions. From early December, the elite triathletes and cyclists began heavy training for the upcoming national competitions commencing in mid-January. The elite athletes would travel to the next competition venue a few days in advance, returning to their training base in southeast Queensland immediately after the race. In March, five elite triathletes participated in the ITU Oceania Regional Triathlon Championship race in Queenstown, New Zealand. All the recreational triathletes and cyclists maintained regular training and competed in local and state-level competitions.

At baseline and follow-up, subjects were asked to report for testing between 0500 and 0900 h after an overnight fast, having refrained from exercise for the previous 24 h. Blood and saliva samples were collected, with the subjects having rested in a seated or supine position for at least 10 min before sampling, after which they completed the Wisconsin Upper Respiratory Symptom Survey (WURSS-44) (3). All subjects were asked to complete a daily exercise training diary throughout the study period.

Identification of infection and illness

For a URI episode to be recorded, subjects must have had upper respiratory signs and symptoms for $\geq$ 48 h. Subjects were asked to contact the chief investigator (L.S.) if they experienced two or more of the following upper respiratory signs and symptoms continuously for a minimum of 24 h: sore throat, runny nose (rhinorrhoea), cough, scratchy throat, nasal congestion, headache, fever, hoarseness, sneezing, and/or body aches and pains. We asked all symptomatic subjects to contact us once symptoms were continuous for 24 h to appropriately manage the episode. Asking the subjects to contact us as early as possible also helped to ensure that the WURSS-44 survey was completed on a daily basis for the duration of the illness. Subjects in whom signs and symptoms did not persist for $\geq$ 48 h were considered to not be suffering from a URI, and, therefore, samples and data collected were excluded from all analyses. Particular care was taken to assess and exclude subjects with itchy eyes and sneezing, with or without a history of allergy. If in doubt, pathology samples were collected and subjects were closely monitored for the following days for a more substantial clinical picture to develop. Pathology tests and clinical examination for acute allergy diagnosis were ordered if indicated.

For each URI episode, the chief investigator visited the subject within 24–36 h of the commencement of symptoms to collect nasopharyngeal and throat swabs, a saliva sample, and a venous blood sample. Wherever possible, samples were collected between 0500 and 0900 h in accordance with baseline and follow-up collection times. To monitor for possible complications of upper respiratory episodes, subjects were examined clinically and were monitored via telephone for the duration of the episode. If additional non-URI symptoms were reported, or if the subject or chief investigator was unduly concerned, the subject was immediately referred to one of the study's physicians for further evaluation.

Nasopharyngeal and throat swabs

After a thorough clinical examination, nasopharyngeal and throat swabs were collected from all consenting subjects who reported a URI. For nasopharyngeal collection, a flexible, cotton-tip, twisted aluminum wire–shaft swab (orange top) (Copan Italia, Brescia, Italy) was gently passed through the nostril until resistance at the posterior nasopharynx was encountered. For the throat swab collection, both a cotton-tipped soft plastic–shaft swab (green top) and an orange-top swab were passed through the mouth and rubbed over the tonsils and oropharynx. The orange-top swab was immediately placed in viral transport media (VTM), whereas the green-top throat swab was placed in Amies agar gel transport medium without charcoal. All swabs were transported under refrigerated conditions to the laboratory for immediate processing.

Orange-top swabs in VTM were forwarded to the Queensland pediatric infectious diseases laboratory at Sir Albert Sakzewski Virus Research Centre, Royal Children's Hospital, Brisbane, Australia for batch storage at −70°C awaiting nucleic acid preparation. After thawing, nucleic acids (200 μL) were extracted from each swab using the High Pure Viral Nucleic Acid kit (Roche Diagnostics, Castle Hill, Australia) following the manufacturer's instructions. Nucleic acid extracts were stored at −70°C until the PCR detection protocols were performed for (i) adenovirus, influenza A and B viruses, parainfluenza viruses 1, 2, and 3, and respiratory syncytial virus (32); (ii) human metapneumovirus (15); and (iii) human rhinovirus, human coronavirus 229E and OC43, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Bordetella pertussis* (including parapertussis) (10). Individual viral target sensitivity (limit of detection) and specificity are as follows: respiratory syncytial virus: 10 gene copies, 99.5%; influenza A and B viruses: 50 gene copies, 98.2%; parainfluenza virus 1: 50 gene copies, 95.5%; parainfluenza virus 2: 100 gene copies, 96.3%; parainfluenza virus 3: 10 gene copies, 98.0%; adenovirus: 5 gene copies, 99.0%; human metapneumovirus: 20 gene copies, 96.0%.

Green-top swabs in Amies agar gel transport medium without charcoal were forwarded to the microbiology department at Sullivan Nicolaides Pathology, Brisbane, Australia for immediate standard microscopy and culturing for the detection and identification of potential bacterial respiratory pathogens, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Streptococcus pyogenes*, *Moraxella catarrhalis*, and *Enterococcus spp*. Antibiotic sensitivity was also determined.

Serological testing

Detection of antibodies against EBV (anti-EBV nuclear antigen IgG antibodies, antiviral capsid antigen IgG and IgM antibodies), cytomegalovirus, and herpes simplex virus types 1 and 2 were measured by ELISA and immunofluorescent antibody methods using inhouse kits approved for diagnostic use in Australia by the Therapeutic Goods Administration. Serological status was determined at baseline, at each URI episode, and at follow-up.

Other events

Other medical episodes such as gastrointestinal symptoms or bone, joint, or muscular ailments (including sports- or training-related injuries) without upper respiratory symptoms were not included as illnesses in these analyses.

Illness survey

The WURSS-44 (3) was used to comprehensively assess the daily symptomatology and functional impairment for the duration of each URI episode. The WURSS-44 includes one global severity question, 32 symptom-based questions, 10 functional impairment/quality-of-life questions, and one global change question (Table 1). Subjects were asked to complete the WURSS-44 each day until complete resolution of the illness episode was indicated by answering "not sick" to the single global severity-of-illness question. The severity of each reported symptom was rated on a seven-point Likert scale: 1 (very mild), 3 (mild), 5 (moderate), and 7 (severe). Symptoms not experienced were recorded as 0. An overall symptom score was calculated by adding the severity scores from the first 43 items. An asymptomatic period of at least 7 d was required for a subsequent episode to be classified as a new illness. If upper respiratory symptoms reappeared within 7 d of initial resolution, this observation was classified as a reoccurrence or complication of the primary episode and was included in the duration of the previous illness. For calculation of rates of illness, subjects were considered at risk of a new illness during the entire surveillance period minus the duration of each illness episode, and minus 7 d after each episode. Questions relating to the use of any dietary supplements, ergogenic aids, or medications (prescribed or over the counter) that may have influenced underlying immune function, exercise capacity, or symptom progression were added to the WURSS-44 form.

The term "URI" was used to define the constellation of signs and symptoms that primarily affect the upper airways. For clarity, where the origin of the dysfunction was caused by an identifiable pathogen, the problem was categorized as a URTI. In cases where no known cause was found (i.e., no identifiable pathogen or agent was detected), the problem was categorized as an unidentified URI (U-URI) because we could not exclude the possibility that an unidentified pathogen might have been the causative agent.

Measures of training

All athletes were requested to maintain their normal training and competition programs throughout the 5-month study period. For each session, type of activity, training distance (km), duration (min), and intensity (scored on a 1–5 Likert scale; 1: easy, 5: maximal) were recorded in a daily training diary. Session details (e.g., hill runs, interval session, long-distance effort, race), illness/injury ratings (scored on 0–3 scale; 0: no illness/injury, 3: severe (e.g., discontinued training/work)), general comments on how the subject was feeling, and previous night's sleep (h) were also recorded daily. Exercise energy expenditure was estimated from training diary data using METs. One MET is defined as energy expenditure at rest (i.e., approximately 3.5 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$, or 1 $kcal \cdot kg^{-1} \cdot h^{-1}$). MET values for various types and intensities of activities were obtained from the compendium of physical activity (1) coding scheme, and the product of the duration of that activity (in minutes) and the assigned MET value was used to estimate an energy expenditure value in MET-minutes. Individual weekly totals were calculated by summing all MET-minutes for activities undertaken during a 7-d period.

Statistical analysis

The sample size of 36 subjects per group was calculated, assuming a type I error of 5% and power of 80% to detect a

TABLE 1. Symptom and functional impairment questions of the Wisconsin Upper Respiratory Symptom Survey (WURSS-44).

Symptoms[a]	Symptoms	Symptoms	Functional Impairment[b]
1. How sick do you feel today?	12. Body aches	23. Swollen glands	34. Think clearly
2. Cough	13. Feeling run down	24. Plugged ears	35. Speak clearly
3. Coughing up stuff	14. Sweats	25. Ear discomfort	36. Sleep well
4. Cough interfering with sleep	15. Chills	26. Watery eyes	37. Breathe easily
5. Sore throat	16. Feeling feverish	27. Eye discomfort	38. Walk, climb stairs, exercise
6. Scratchy throat	17. Feeling dizzy	28. Head congestion	39. Accomplish daily activities
7. Hoarseness	18. Feeling tired	29. Chest congestion	40. Work outside the house
8. Runny nose	19. Irritability	30. Chest tightness	41. Work inside the house
9. Plugged nose	20. Sinus pain	31. Heaviness in chest	42. Interact with others
10. Sneezing	21. Sinus pressure	32. Lack of energy	43. Live your personal life
11. Headache	22. Sinus drainage	33. Loss of appetite	44. Compared with yesterday, I feel …

[a] Symptom-based questions (2–33) ask respondents to "Please rate the average severity of your cold symptoms over the last 24 h by marking the appropriate circle for each of the following symptoms."
[b] Functional impairment questions (34–43) ask: "Over the last 24 h, how much has your cold interfered with your ability to…"

TABLE 2. Selected baseline descriptive characteristics of subjects.

	Elite (*N* = 32)		Recreationally Competitive (*N* = 31)		Sedentary Control (*N* = 20)		
	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	*P*
Age (yr)	22.5 ± 3.8	18.0–34.1	25.2 ± 3.6	18.8–33.8	23.0 ± 3.0	19.0–28.5	0.008
Height (m)	1.74 ± 0.08	1.61–1.89	1.77 ± 0.08	1.63–1.94	1.74 ± 0.08	1.60–1.87	0.239
Weight (kg)	64.8 ± 8.9	51.0–82.0	68.8 ± 10.3	46.2–83.1	71.7 ± 12.3	51.0–89.9	0.060
BMI ($kg \cdot m^{-2}$)	21.2 ± 1.4	18.0–25.9	21.8 ± 1.9	17.3–25.9	23.3 ± 3.5	17.0–29.4	0.001
No. (%) of males	17 (53)		18 (58)		9 (45)		

two-episode difference in the rate of URI. Frequency distributions of all continuous variables were examined to detect outlying values, and the Kolmogorov–Smirnov test was used to test for normal distribution of variables. For normally distributed variables, all descriptive data are presented as either mean ± standard deviation (SD) or mean ± 95% CI unless otherwise stated. Where assumptions for normality could not be met, data were log transformed before statistical analysis. All log-transformed data were back transformed for reporting geometric mean values. Incidence rate ratios (number of new illnesses or infections per person-days at risk) were used to compare the risk of illness or infection in the three groups, using data from the recreationally competitive athletes as the referent category. Means (both arithmetic and geometric) and changes over time were compared using one-way analysis of variance with the Tukey *post hoc* test employed to identify significant differences. Assumptions of homogeneity and sphericity in data were checked, and, where appropriate, adjustments to the degrees of freedom were made using the Greenhouse–Geisser method of correction. For all statistical tests, two-tailed *P* values of less than 0.05 were considered significant. All statistical analyses were performed using SPSS version 13.0 (Chicago, IL).

RESULTS

Descriptions of the subjects

Eighty-three subjects provided informed consent to participate and completed the baseline data collection. Details of age, sex, height, and mass are shown in Table 2. The mean age of the recreationally competitive cohort was slightly older than both the elite and sedentary control groups. Compared with both athlete groups, the sedentary controls had a significantly higher BMI. However, with the exception of one control subject, all were in the healthy BMI range (18.5–24.9). Of the original 83 participants, 17 elite athletes, one recreational athlete, and two sedentary controls withdrew from the study during the 5-month surveillance period. The reasons for withdrawal from the study were unexpected overseas departure ($N = 6$), noncompliance with the study protocol ($N = 11$), serious illness ($N = 1$), and loss to follow-up ($N = 2$). Data from these participants were included in analysis until the point of withdrawal.

Patterns of training

Typical levels of weekly exercise energy expenditure, determined on the basis of data from subjects who returned all three diaries in each of the three groups, are shown in Figure 2. As expected, weekly exercise energy expenditure was highest in the elite group, with values for the recreationally competitive group well above those of the sedentary controls. After week 19, weekly exercise energy expenditure in the elite athletes was more than 50% lower than in weeks 1–18 because of the completion of the national elite competition series.

Pattern and etiology of illness episodes

Evidence for viral and bacterial infections was found in only 11 of 37 (~30%) illness episodes (Table 3). The most common identifiable pathogen was rhinovirus. Evidence of dual infection was found in three episodes, with adenovirus present in two of these. Almost three quarters of the subjects who reported a URI episode tested negative for detectable infectious agents by microscopy, culture, PCR, and serological testing. The highest cluster of episodes occurred for the athletes during the heavy training period of the study in December and January. The five elite triathletes who traveled to Queenstown, New Zealand for an international race did not report any signs or symptoms of URI for the preceding 7 d or the following 14 d on return.

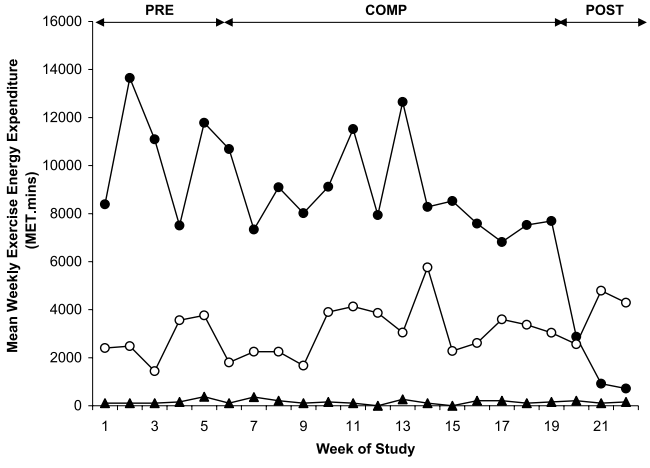

FIGURE 2—Typical weekly exercise energy expenditure. Results are based on complete diary data for elite athletes (*closed circles*), recreationally competitive athletes (*open circles*), and sedentary controls (*closed triangles*). PRE, preseason heavy training; COMP, triathlon and cycling competition series; POST, postseason light training.

TABLE 3. Individual details by cohort for the patterns of upper respiratory illness episodes.

Subject	Sex	Age	Month	Pathogen
Elite				
K 39	Male	18.6	December	HRV
G 29	Female	25.1	December	
G 27	Female	26.9	December	
M 59	Male	18.5	December	
K 38	Female	24.0	December	ADV+ Strep
M 55	Female	18.9	December	
E 22	Female	20.7	December	HRV
E 23	Female	22.1	December	
M 59	Male	18.5	December	PINF3+ NTHI
D 21	Female	20.7	December	
G 27	Female	26.9	January	
S 70	Female	27.2	February	
B 05	Male	22.0	February	Staph (coag+)
B 04	Male	20.7	March	EBV
C 13	Female	19.0	March	
C 08	Female	22.0	March	
E 22	Female	21.0	April	
K 38	Female	24.3	April	
C13	Female	19.0	April	
K 37	Male	23.7	April	
E 22	Female	21.0	April	
Recreational				
L 44	Female	24.6	December	
L 47	Female	24.2	January	
S 69	Female	26.0	January	HRV
S 72	Male	21.3	February	MYC
L 45	Male	25.4	March	
S 69	Female	26.2	March	
A 01	Male	25.4	March	ADV+ HRV
Control				
K 40	Female	20.2	December	
F 24	Female	20.0	January	
W 82	Male	26.0	January	
A 03	Female	24.1	January	HRV
C 10	Male	21.7	January	
B 06	Female	19.6	January	
K 40	Female	20.4	February	
S 74	Male	26.4	March	
K 40	Female	20.6	April	HRV

ADV, adenovirus; EBV, Epstein–Barr virus; HRV, human rhinovirus; MYC, *Mycoplasma pneumoniae*; NTHI, nontypeable *Haemophilus influenzae*; PINF-3, parainfluenza virus type 3; staph (coag+), *Staphylococcus aureus* (coagulase positive); Strep, *Streptococcus pyogenes* (group A).

The numbers of URI episodes in the three groups during the 5-month surveillance period are shown in Figure 3. In total, there were 37 illness episodes in 28 subjects, with seven subjects (five elite, one recreationally competitive, and one control) suffering more than one episode. Overall, elite athletes accounted for 57% of all cases, but a pathogen was identified in only 29% of these cases.

Incidence rate ratios were calculated to compare rates of illness in each group, using the recreationally competitive athlete group as the referent category (Fig. 4). These data show that the elite athletes had higher rates of illness (311 total sickness days) than recreationally competitive athletes (92 total sickness days) and sedentary controls (137 total sickness days) across all three descriptive categories (URI, U-URI only, and URTI only). The differences were only statistically significant for URI and U-URI. The mean duration of U-URI episodes (N = 26) was 6.5 ± 3.2 d (95% CI: 5.2–7.8 d), whereas the mean duration of infectious URTI episodes (N = 11) was 9.6 ± 2.4 d (8.0–11.3 d) (P = 0.006). All episodes, irrespective of etiology, had durations of ≥ 3 d.

During the study, six subjects were treated with antibiotics by the study's infectious diseases physicians: one subject had acute tonsillitis and bacteriological confirmation of *S. pyogenes* (group A) infection; two subjects had symptoms indicative of acute bacterial sinusitis; one developed a severe upper respiratory episode with a dual infection of nontypeable *H. influenzae* and parainfluenza 3; and one developed acute gastrointestinal symptoms from a serious *Campylobacter jejuni* infection, requiring hospitalization. With the exception of these six subjects, all recovered uneventfully without antibiotics, including those patients with suspicion of bacterial etiology.

Symptom survey data

Patterns of symptoms and functional impairments from the WURSS-44 are shown in Figure 5. Across all measures of symptom severity and functional impairment, subjects suffering from a URTI (N = 11) had significantly higher scores than those with a U-URI (N = 26) (all $P < 0.05$) on days 3 and 4 (Fig. 5A). There were no substantial differences between these two groups in symptom scores on days 1 and 2. The elite athletes (N = 21) as well as the sedentary controls (N = 9) demonstrated higher mean WURSS-44 scores than the recreationally competitive athletes (N = 7) on the first 4 d of illness (Fig. 5B), regardless of etiology.

Mean number of symptoms across the entire duration of illness in the U-URI group was 17.1 ± 6.0 (95% CI 14.7–19.5) and in the URTI group was 21.8 ± 5.7 (18.0–25.7) (P = 0.034). There was no difference between the two groups in the mean number of functional impairment parameters (U-URI group, 6.5 ± 2.7 (5.5–6.6); URTI group, 6.8 ± 3.2 (4.7–9.0); P = 0.79).

DISCUSSION

To our knowledge, this is the first study to have comprehensively investigated the incidence of URI and the pathogenic etiology and symptomatology of URI in

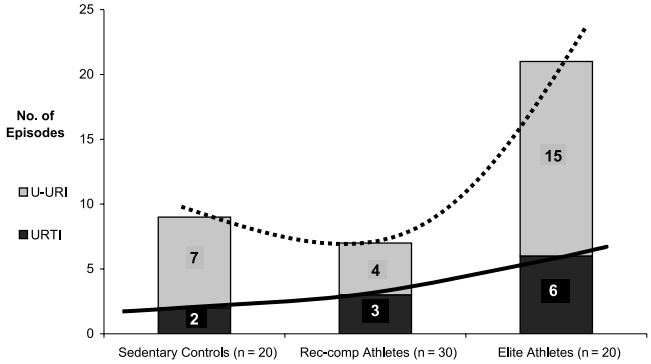

FIGURE 3—Number of episodes of unidentified upper respiratory illnesses (U-URI) and upper respiratory tract infections (URTI) during the 5-month surveillance period. *N*, number of subjects in each cohort available during the surveillance period.

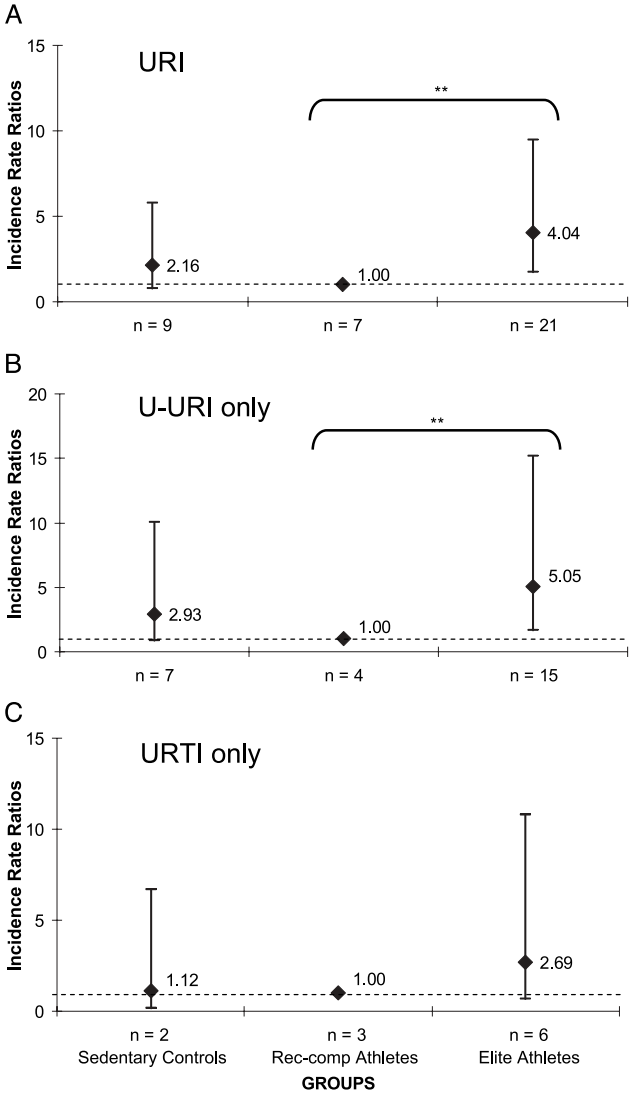

FIGURE 4—Mean (95% CI) incidence rate ratios for (*A*) URI, (*B*) U-URI–only, and (*C*) URTI-only episodes, comparing recreationally competitive athletes (referent category) with sedentary controls and elite athletes. *N*, number of episodes. ** Statistically significant difference between groups.

elite and recreationally competitive athletes for an extended training and competition period. The results confirm that, during an entire competitive season, there is a J-shaped relationship between volume and intensity of training and URI incidence, with lower rates of illness observed in the recreationally competitive athletes, and substantially higher rates in the elite triathletes and cyclists (21,24). However, the results also strongly suggest that not all upper airway illnesses, ubiquitously described in previous literature as ''infections'' or URTI, are associated with the common identifiable respiratory pathogens. Detailed follow-up of symptomatic URI episodes in elite athletes revealed that only 30% of such episodes had been caused by an identifiable pathogen. The data also indicate that symptoms of a URTI episode are more severe on days 3 and 4 of illness. These findings provide direction for the management and treatment of URI symptoms in individuals undertaking regular exercise at the recreational and elite levels.

Although we were unable to identify a pathogen in many cases of illness despite comprehensive laboratory investigations, the WURSS-44 data confirmed that illness symptoms were very similar in both URTI and U-URI in the first 2 d of illness. However, in those illnesses for which a pathogen was subsequently identified, symptoms were significantly worse on days 3 and 4 of the URTI, and the episode duration was about 3 d longer. These findings suggest that there may have been a higher degree of immunological and inflammatory activation, presumably as a result of the initial microbial assault, in those cases where a pathogen was identified.

Our findings raise the issue of the cause of the unidentified illnesses. Given that symptoms for the U-URI were similar to those of the URTI on the first 2 d and that the U-URI lasted for about a week, we are confident the participants in all three groups who had U-URI were actually ill. However, although it is possible that our identification methods may have failed to detect some pathogens, other etiologic studies (19,31) employing very similar methods have reported high (> 55%) proportions of illnesses without an identifiable pathogen. One possible explanation for the lower positive yield is that respiratory pathogen detection (particularly viruses) in Queensland, Australia peak in winter (May–August) (31), which is outside the period of this study. In addition, newly identified viruses, including human bocavirus, and human coronaviruses NL63 and HKU1 in upper respiratory specimens (2,31), highlight the potential for previously unknown pathogens to cause illness.

More research is required to identify the inflammatory mechanisms (e.g., changes to the nasopharyngeal mucosal lining or in the normal commensal flora) or mediators of the symptoms of U-URI reported by athletes. Specific investigations exploring special epithelial and vasomotor features of the U-URI symptomatology in comparison with that of URTI subjects is of particular interest. Information is needed on the underlying immune control processes that regulate noninfectious inflammatory protection for host tissues, the development of more effective laboratory investigations, and the effectiveness of therapeutic and other interventions.

For the illnesses with identifiable pathogens, rhinovirus was the most commonly identified, with relatively small numbers of bacterial pathogens, including *S. pyogenes* (group A) (a frequent cause of tonsillitis, more commonly known as strep throat), *H. influenzae*, *Staphylococcus aureus*, and *M. pneumoniae*. These findings are consistent with previous general population URI studies (17). Primary EBV infection was identified in a single case. It is interesting to note that herpesviridae shedding, particularly EBV, has been implicated as a cause of significant URI symptoms in conditioned athletes during intensive training

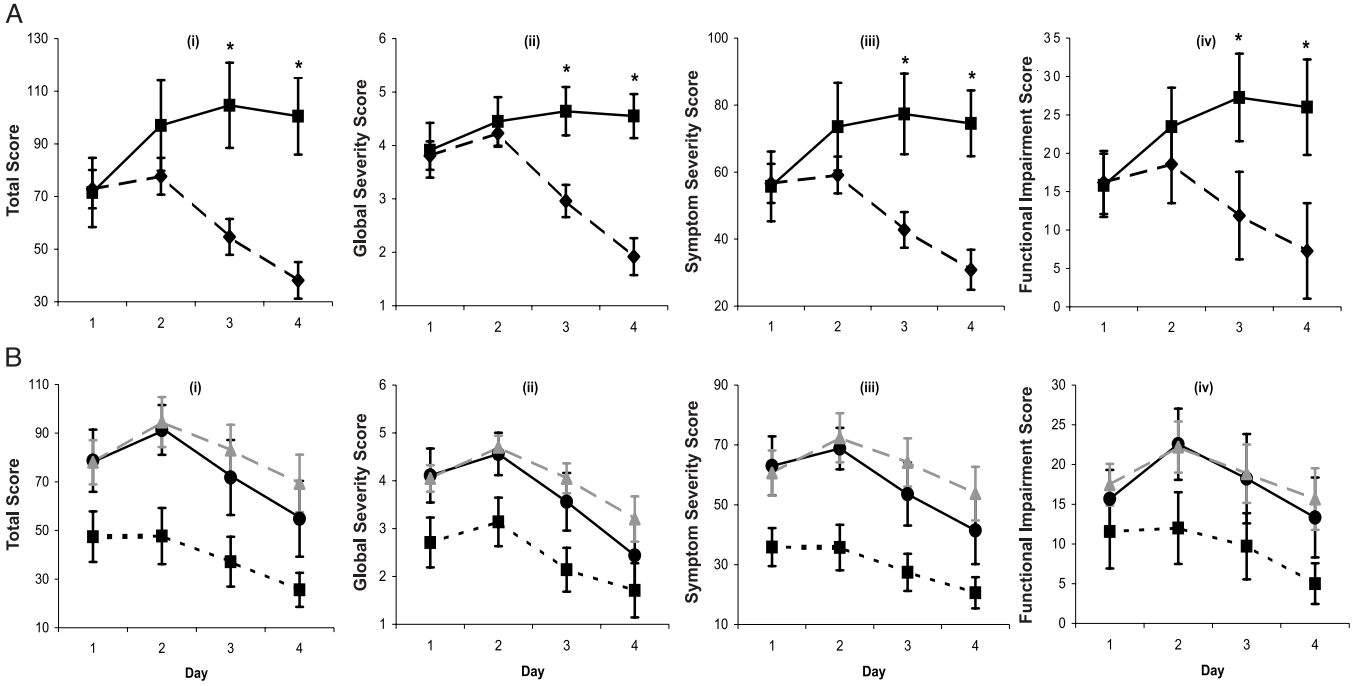

FIGURE 5— *A*, Mean (± SEM) WURSS-44 scores over time for U-URI (*N* = 25) vs URTI (*N* = 11) episodes. *B*, Mean (± SEM) WURSS-44 scores over time for elite (*N* = 20) vs recreationally competitive (*N* = 7) vs control (*N* = 9). i, Total score; ii, global severity score; iii, symptom score; iv, functional impairment score. * *P* < 0.05. *Black squares with solid lines*, URTI; *black diamonds with dashed lines*, U-URI; *gray triangles with dashed lines*, elite athletes; *black squares with dotted lines*, recreationally competitive athletes; *black circles with solid lines*, controls.

periods (12). As yet, we have not undertaken EBV DNA (or any other herpesviridae group) analysis, though it is plausible that some of the U-URI symptoms might be associated with latent viral shedding. As with influenza, primary EBV virus infection may be considered a systemic condition with significant upper respiratory involvement.

Most of the illnesses in the elite athletes occurred during the heaviest training periods, with symptoms usually lasting for approximately 1 wk. These findings on the pattern of illness in relation to training are consistent with previous reports (22,23). In our study, the average duration was significantly longer for episodes with an identifiable pathogen, and the WURSS-44 symptom data indicated that the elite athletes reported greater functional impairment and loss of quality of life (WURSS-44 scores) than the recreational athletes across all parameters. Given the possible negative effects of illness on training and competitive performance, the greater reported functional impairment in the elite athletes might relate to a higher intrinsic sensitivity to the presence of illness symptoms. Coaches and athletes should be reminded that this period may coincide with key training sessions or a game or tournament, and a clinical decision may be necessary to determine whether the athlete's participation in training or competition can be maintained. Athletes should be educated on the importance of self-monitoring for resolution of symptoms during illness. During these episodes, physicians, coaches, and athletes should discuss the time course and pattern of the athlete's (graded) return to a full training program to promote recovery, minimize complications, and prevent possible contagion.

Although the elite athletes were more likely to experience an upper respiratory *illness* during the study, we were unable to demonstrate any differences in the rate of *infectious* episodes. This finding might reflect the low numbers of *identified* URTI (only 11 in total), giving only limited power to detect between group differences. We had initially estimated that our sample size of 36 in each group would provide sufficient power to detect group differences, but the proportion of illnesses in which an identifiable pathogen was identified (only 6 of 21 in the elite group) was lower than in previous studies of general populations, which have suggested that 60–70% of illnesses have a causative identifiable pathogen (17). Although the small number of infections is a limitation of this study, few previous studies have identified the pathogens associated with URI in athletic populations.

The main strength of the study is that we collected prospective data during an entire elite-level competitive season, using objective measures for determining the etiology of symptomatic URI. The study design was strengthened by the inclusion of three cohorts with distinctly different levels of exercise and training. Presumably because of the logistic difficulties associated with collection of samples during an entire competitive season, few other studies have attempted to do this. Although other studies have followed cohorts for longer periods (e.g., Matthews and colleagues (18) tracked their participants for 1 yr) or have included larger numbers of athletes (e.g., Nieman et al. (22,23) surveyed several hundred athletes after a single running event), these studies have relied on

participant recall of having had a common cold, flu, or allergy for periods ranging from 1 d to 6 months (18,20), and some have asked physicians to verify episodes of illness (16). Unfortunately, the early signs and symptoms of URI, whether caused by bacteria or viruses, can be remarkably similar. So, too, can the symptoms of allergic, cold dry air inhalation, inflammatory, vasomotor, and other idiopathic upper respiratory disorders seen in athletes that are often unrelated to a disease-causing pathogen and are difficult to differentiate on a clinical basis alone. However, in this study, we collected blood and saliva samples, took swabs at the time of the illness, and used a comprehensive range of pathogen-detection procedures to identify the underlying microorganism for each illness episode. To our knowledge, this is the first study to have used objective laboratory methods and symptom diaries to describe the pathogenic etiology and symptomatology of URI in elite athletes.

Our results suggest that URI should not be ubiquitously termed ''infectious'' and that further research is necessary to better understand the relationship between exercise volume, intensity, and load with pathogenic etiology of URI in elite athletes. In terms of medical management of athletes with URI, these findings suggest that in the absence of objective measures for detecting pathogenic microorganisms, it might be helpful to have athletes keep WURSS-44 symptom diaries for the first 4–5 d of a URI episode, so that those with persisting high levels of symptoms can be managed and subsequently assessed for an infectious episode. Physicians should now consider both infectious and noninfectious causes when symptomatic athletes present to their clinic with URI symptoms. Research must continue to define the variable etiologies of URI observed in athletes and to refine diagnosis, treatment, and management strategies for physicians, coaches, sports scientists, and the athletes themselves.

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