Vaccine-Preventable Adenoviral Respiratory Illness in US Military Recruits, 1999-2004

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Vaccine-preventable adenoviral respiratory illness in US military recruits, 1999-2004

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Abstract

Background and Methods: The high burden of respiratory infections in military populations is well documented throughout history. The primary pathogen responsible for morbidity among US recruits in training was shown to be adenovirus. Highly efficacious oral vaccines were used for 25 years, but vaccine production ceased in 1996, and available stores were depleted by early 1999. Surveillance for acute febrile respiratory illness was performed at eight military recruit training sites throughout the United States from July 1999 through June 2004 to document rates after loss of the vaccines. Laboratory diagnoses complimented the surveillance efforts.

Results: Over the 5 years, nearly 12 million person-weeks were followed and an estimated 110,172 febrile respiratory illness cases and 73,748 adenovirus cases were identified. Rates of illness were highest at the Navy and Air Force training centers, with average annual rates of 1.20 and 1.35 cases per 100 recruit- weeks respectively. Adenoviral-associated illness rates peaked in weeks 3 to 5 of training, depending upon service.

Conclusions: The burden of adenoviral illness among US recruit populations has returned to high levels since loss of the vaccines. Restoration of an effective adenovirus vaccine effort within the military is anticipated by 2008, potentially reducing the adenovirus morbidity suffered in this vulnerable population. Efforts to determine the burden of adenovirus and potential benefits of vaccination in civilian populations are being renewed.

Keywords

adenovirus vaccine; military recruits; respiratory illness rates; adenovirus respiratory illness

1.0 INTRODUCTION

Military populations throughout the world and throughout history have suffered considerable morbidity from respiratory infections. In the US military, these cases have been called acute respiratory disease (ARD), acute respiratory illness, and febrile respiratory illness (FRI). For the sake of clarity, the term “FRI” will be used in the remainder of this paper. Close living conditions, environmental exposures, physical challenges, stress, constant introduction of immunologic naives, and hygienic challenges are considered important factors that make military populations vulnerable to infectious diseases [1-3].

Studies during the 1950s and 1960s documented the epidemiology of respiratory illnesses in the military, noting that recruits in initial training experienced higher rates of illness than “seasoned” personnel [3,4]. With the discovery and characterization of adenoviruses in 1953 [5,6], and subsequent demonstration of seroconversion to this virus among those symptomatic [7], up to 70% of respiratory illness in recruits was finally linked to an etiologic agent [8-13]. Adenovirus serotypes 4 and 7 were recognized as the most important strains responsible for respiratory disease in recruit populations [9,13-15]. In addition to the morbidity and occasional mortality suffered by the recruits, distraction from the regimented training program was recognized as mission compromising and costly to the US government. Affected recruits often required a period of convalescence, lengthening their training time and likely increasing virus transmission to newer cohorts as they resumed training [16].

The impact of adenoviruses on recruit populations stimulated the development of vaccines. Inactivated parenteral vaccines were first investigated, but concerns over the oncogenic potential of some contaminating agents in the cell lines used for growth of the adenoviruses (recently found to be unsubstantiated [17]) hampered these efforts [18,19]. Subsequent attempts at intestinal infection with live wild adenovirus strains was found to yield high rates of seroconversion with few adverse effects, including very little transmission to closely associated unvaccinated individuals [18-24]. However, introduction of the type 4 oral vaccine alone resulted in increased incidence of type 7 associated disease [20,25]. Further study demonstrated that oral adenovirus vaccines directed against both serotypes 4 and 7 were not only safe, but highly effective in reducing disease in recruits [23,25-29]. Routine vaccination with the oral adenovirus 4 and 7 vaccines began at US recruit training camps in 1971. Rates of adenoviral illness were subsequently reduced by up to 96% [16,20,30].

Several cost-benefit analyses have demonstrated the benefits of the adenovirus vaccination program [31-33]. The first, published in 1973, estimated cost savings for the Army during the years 1970 and 1971. It was estimated that the vaccines prevented 26,979 cases of FRI within the Army over the 2 years at a cost of $279 per illness, for an ultimate savings over vaccination program expenses of $2.6 million [31]. A second Army study was performed in 1998. Using hospitalization data, 2.6 cases of FRI per 100 recruit-weeks were estimated to be vaccine preventable. Translated, 12,370 cases of FRI occurred annually among Army recruits, and a year-round implemented vaccination program would prevent 7800 of these cases. Direct and indirect costs were estimated at $2134 per FRI case, with annual vaccination savings estimated at $15.5 million [32]. A third cost-benefit study estimated savings if the adenovirus 4 and 7 vaccines were reacquired and administered at the Navy recruit training facility at Great Lakes, Ill. Published in 2000, this study used the same estimates of vaccine-preventable FRI of 2.6 cases per 100 recruit-weeks, and estimated that 4555 cases of illness could be avoided annually with year-round vaccination. The Navy has not enforced mandatory hospitalization of recruits with FRI, as the Army has largely done, so cost incurred per case took into consideration clinic visits and an FRI hospitalization rate of 7.6%, in addition to the indirect costs. Annual savings to the Navy were estimated at $860 per case, or $2.6 million annually [33].

Despite the success of the adenovirus vaccination program, production of the vaccines by the sole manufacturer ceased in 1996. Attempts to reach an agreement suitable to the Department of Defense and the vaccine manufacturer for continued production were unsuccessful. Seasonal rationing of remaining vaccine stores occurred until depletion in early 1999. During this transition period, the Naval Health Research Center (NHRC), San Diego, Calif, instituted surveillance at 5 sites in 1996, then expanded to 8 military recruit training centers in 1998.

The standardized surveillance results from the 8 recruit training centers during the 5-year period from July 1999 to June 2004 are presented here. The objective was to define the pathogen-specific FRI rates and site-specific trends in this vulnerable population.

2.0 METHODS

The definition of a case of FRI is a recruit presenting for medical care with an oral temperature ≥38°C (100.5°F), plus any respiratory symptom, such as cough or sore throat. All clinical pneumonias are included in the case definition. Since 1998, this standardized surveillance network has included Great Lakes Naval Training Center in Illinois, Fort Leonard Wood Army Training Center in Missouri, Fort Jackson Army Training Center in South Carolina, Fort Benning Army Training Center in Georgia, Cape May Coast Guard Training Center in New Jersey, Marine Corps Recruit Depots in California and South Carolina, and Lackland Air Force Training Center in Texas. Length of basic (initial entry or boot) training is 8 weeks for the Army, 7 weeks for the Navy, 6 weeks for the Air Force, 12 weeks for the Marine Corps, and 8 weeks for the Coast Guard.

Each training site except Cape May had an NHRC staff member dedicated to conducting the surveillance. Staff collected numerator data (individuals meeting the case definition) and denominator data (total recruit population at each site), and calculated weekly rates of FRI. A convenience sampling of approximately 10 recruits per site per week presenting to the medical clinic and meeting the FRI case definition was performed. Throat swabs were taken and a questionnaire completed. Throat swab specimens were collected in viral transport medium, Micro Test™ Multi-Microbe Media (REMEL, Lenexa, KS) and stored at−70°C within 60 minutes. Collected specimens were sent to the Navy Respiratory Disease Laboratory at NHRC on dry ice for viral culture on a periodic basis, not to exceed 1 month. This Laboratory is College of American Pathologists accredited with Clinical Laboratory Improvement Program certification [34]. Samples received were processed in two cell lines permissive to growth of adenovirus, influenza A, influenza B, parainfluenza viruses, enteroviruses, and respiratory syncytial virus. Percentages for each diagnosed pathogen were calculated and then extrapolated to the total FRI cases to estimate the pathogen-specific burdens for each site. Using the denominator data, estimated rates of pathogen-specific disease were also calculated. Only adenovirus-associated illness data are presented here. Linear modeling was performed to compare monthly rates of adenovirus illness at different sites, and investigate differences in adenovirus rates between years. Binomial probability was used to compare the peak rate observed at Great Lakes with peak monthly rates observed at other sites. Correlation coefficients were calculated for trends observed in between rates and population size and between rates and average ambient temperatures at the Army Ft. Jackson training center.

2.1 Laboratory Processing

Cultures were performed using previously described procedures [35,36] using two different cell lines. For adenovirus culture, throat specimens collected from individuals with FRI were inoculated into duplicate A549 (Human Lung Carcinoma) cell culture tubes (Diagnostic Hybrids, Inc., Athens, OH), after washing with basic Eagle's minimum essential medium with Earle's balanced salt solution, without L-glutamine (Cambrex, Walkersville, MD). After inoculation, the cells were incubated for an adsorption period of 1 hour at 37°C (35-38°C).

Maintenance medium with 2% fetal bovine serum was then added and the cells were incubated at 37°C (35-38°C). Re-feeding of the cells with this maintenance media (media change) was performed on days 1 and 7. Cultures were observed for evidence of virus replication and resulting cytopathic effect (CPE) for a period of up to 14 days. Once viral CPE (3-4+) was observed, isolates were identified with monoclonal antibodies (CHEMICON International, Inc., Temecula, CA) through immunofluorescence staining.

A 20% random selection of adenovirus isolates recovered from sampled recruits with FRI were serotyped using a modified version of the conventional tube neutralization test with flat-bottom 96-well microplates (type-specific rabbit hyperimmune sera to adenoviruses 1-5, 7, and 21, provided by Dr. David Schnurr, Viral and Rickettsial Laboratory, California Department of Health Services, Berkeley, CA) [37]. Beginning in 2002, serotypes were determined through molecular serotyping methods validated against the microneutralization gold standard above [38,39].

3.0 RESULTS

Among all FRI cases sampled, the percentage confirmed to be adenovirus ranged from 52.3% to 76.4% of total FRI cases. The next most commonly diagnosed pathogen was influenza A. During the 5-year period, an estimated 73,748 cases of adenoviral illness occurred at these 8 recruit training centers, for an annual average of 14,750 cases. Total FRI cases, FRI rates, and estimated adenoviral cases at each training center are presented in Table 1. Nearly 12 million recruit-weeks were followed over the 5 years, with the identification of 110,172 FRI cases. Average site-specific FRI rates ranged from 0.34 to 1.35 cases per 100 recruit-weeks over the 5-year surveillance period. The FRI rates at the different sites were significantly different from each another ($p<0.0001$), with the exception of Fort Leonard Wood and Fort Jackson.

The annual average number of adenovirus cases in 2003 and 2004 was 33.2% higher than the annual average of the previous 3 years, even though the total population at risk slightly decreased. Adenovirus rates in 2002-2004 were significantly higher than in 1999-2000 ($p<0.05$). The yearly estimated number of adenoviral cases, including maximum and minimum months, is collectively demonstrated in Table 2.

Estimated adenovirus-specific FRI rates are graphically presented in Figure 1. To improve clarity in this figure and because the service specific rates closely mirrored the rates at each individual site (data not shown), data from the 3 Army sites were combined, and data from the 2 Marine sites were combined together. The peak rate of adenoviral illness per 100 recruit-weeks was significantly higher at the Navy site as compared to all other sites ($p<0.0001$). Onset of diagnosed adenoviral illness per training week is presented in Figure 2. The proportions of diagnosed adenoviral cases peaked between weeks 3 and 5 of training. The peak among Army recruits occurred 1 to 2 weeks after that observed for the other services. Difficulty in distinguishing trainees finishing basic training and those starting advanced training probably contributed to unusually high week 9+ numbers at Army sites. Marine recruit training is 12 weeks, so the 9+ week category included a larger susceptible group than the other training sites, explaining the late increases at Marine sites. Week 5 at the Air Force site is spent in field training, where capture of FRI cases was suboptimal.

Only the Army sites annually approached near zero cases of adenoviral illness per 100 recruit-weeks (Figure 1). This can be seen more clearly when rates of illness at the Army sites over the 5-year time period are graphed together with the total complement of recruits in Figure 3. Although cases of FRI continued, almost no cases of adenoviral illness were identified during a short period in January every year at the Army sites.

A weak correlation was observed between FRI rates and the size of the population in training (coefficient of correlation 0.263; Figure 3). To evaluate the historically described inverse relationship between FRI rates and temperature [8,24], mean monthly temperatures and adenovirus-specific FRI rates were compared for the Army's largest basic training center, Fort Jackson, SC. Rates of illness did not increase with decreasing temperature; rather, rates increased during warmer months (coefficient of correlation 0.559). Note that population size is also highest in warmer months at all recruit sites, potentially contributing to this observed correlation.

Almost all of the adenovirus-associated FRI since 1997 has been caused by serotype 4 [40, 41]. Both traditional and molecular methods were utilized to serotype the 20% random subset of adenovirus isolates; approximately 95% were serotype 4 during the 5-year period of surveillance. The majority of the remaining 5% were serotype 3.

4.0 DISCUSSION

The FRI rates observed since the loss of the adenovirus vaccines are similar to rates noted in the literature from the 1950s. Hilleman and colleagues examined adenoviral rates at Fort Dix, NJ, from June 1954 to May 1955. Rates from 0.2 per 100 recruit-weeks during the summer/fall months to 3.4 per 100 recruit-weeks in the winter months were seen [8,42]. Although not a focus of this paper, surveillance was conducted without laboratory diagnostic support among recruits prior to 1997. Using this available data from 3 Army sites, average rates of FRI from January 1995 to June 1997, a period of nearly continuous adenovirus vaccine usage, were compared to rates from January 2002 to June 2004, when the vaccine was no longer available. A greater than 3-fold increase in the FRI rate was observed, from 0.26 to 0.88 cases per 100 recruit-weeks, after vaccine usage ceased. The recently observed FRI rates suggest that during periods of high transmission, up to 30% of the total recruit population is affected (recruits seeking medical care with a fever) by the end of training.

The lack of adenovirus-associated FRI at the Army sites in January of each year is provocative. The Army sends recruits home for the holidays for the last 2 weeks of December. This practice, called “Exodus,” is unique to the Army. Although smaller in numbers, cases of FRI are still captured upon their return, but the percentage of adenovirus contributing to these cases is often zero (Figure 3). Non-Army sites, in contrast, continue to isolate adenovirus from FRI cases during this time period. Although we cannot discount other potential differences between the recruit training centers that could account for this observation, the temporal association with the “Exodus” cannot be ignored. This predictable drop in adenoviral illness at the Army training centers is an observation of this work that warrants further consideration and analysis. Elucidation of behavioral, procedural, or environmental interventions ultimately resulting in sustained reductions of adenoviral illness could result.

A weakness of this study is the difficulty of capturing all recruits with FRI. The numbers presented here are recruits who chose to go to a medical clinic for treatment of their illness. Health care-seeking behavior is required to be captured by our surveillance. Data support the perception of some health care workers that there are strong negative incentives for seeking medical care among recruits trying to get through boot camp. A recent study among Marine recruits demonstrated that only 37.5% (33/88) of recruits with fever and respiratory symptoms, and only 33.3% (26/78) with a confirmed adenoviral infection, sought treatment at the clinic (Russell, submitted). This is consistent with studies by Seal and colleagues at the Naval Training Center Great Lakes in the early 1950s. They found that only 33.0% (297/899) of recruits with ARI (defined as fever of ≥100°F and “generalized involvement of the respiratory tract”) sought medical treatment. In addition, they observed recruits with fevers as high as 103°

F who chose not to seek medical treatment [43]. Similarly, McNamara and colleagues reported that more than 70% of those with adenoviral disease did not present to medical clinics [11].

Given the above, the numbers in Table 1 are conservative. Cases likely missed in the clinic, combined with the probable large number of recruits who chose to avoid health care because of the negative ramifications (such as being removed from training, placement in a medical holding facility, delayed graduation, or potential removal from military service), suggest that many times the number of reported FRI cases actually occurred. We estimate that we could be capturing as few as 1 of every 3 FRI cases. If these estimates are correct, complete capture would result in approximately 66,000 annual cases of FRI in our recruit training centers. Assuming a similar proportion of this total number of FRI cases is caused by adenovirus, the total number of febrile adenoviral cases would increase to 45,000 annually. In addition, not all infections with adenovirus are febrile. Some result in a milder respiratory illness without fever, and some with no symptoms at all [16,44]. Hilleman reported that 20% suffered afebrile respiratory symptoms, and 40% to 50% experienced only very mild or inapparent infections [8,42]. If these afebrile adenoviral illnesses are impacted as well, reinstitution of adenovirus vaccination may provide benefits beyond what has been quantified in this report.

The predominance of serotype-4 during the surveillance period is unlike the serotype distribution historically seen. In addition to serotype-4, serotypes 7, 21, and 3 were commonly seen in the pre-vaccine era [9,15,45]. The small proportion of serotype-3 currently present is randomly distributed over all recruit training centers. Despite the predominance of serotype-4, herd immunity in future years is unlikely to result in decreased transmission, as immunologically naïve recruits arrive daily, maintaining the proportion of susceptibles available for infection. Re-introduction of the adenovirus serotype 4 and 7 vaccines in the future may result in a shift of the predominant serotypes. Surveillance should continue throughout this period.

If assumptions made in the discussed cost/benefit studies still hold, and rates elucidated in this surveillance work applied, the estimated cost of recognized febrile adenoviral disease to the US military would be approximately $21.52 million annually. It should be pointed out that the impact of adenoviral illness on trainees and the training program would extend well beyond this figure, however. Deaths associated with adenovirus have been reported [46-49]. The cost of a death is appropriately debatable and difficult to quantify, and the cost of symptomatic recruits who do not report for medical care is not represented.

4.1 Civilian Relevance

Although the literature on adenoviral infections in immunocompromised populations and people in health care institutions has been growing, the significance of adenovirus-associated respiratory disease in civilian community populations is still unclear. Early studies recognized the significance of serotype 3 among civilians, but found little evidence of illness caused by serotype 4 [50]. This early study estimated that with a low disease burden, a 100% efficacious vaccine would only decrease the number of respiratory illnesses suffered in the <10 years age group by 6%. This was judged an insufficient proportion to recommend vaccination in the civilian sector. More recent reports, although sparse, suggest that serotype 4 comprises 2% to 3% of the adenovirus strains found globally [51,52] and is associated with nosocomial outbreaks [53]. Adenovirus serotype 7, in contrast, comprises up to 20% of all reported adenovirus strains globally [51], is associated with numerous documented outbreaks [54-56], and is an important pathogen resulting in serious illness in children younger than 5 years of age [57-59]. It is felt, however, that the true incidence of adenovirus serotype 4 and serotype 7 disease is unknown and probably underestimated in civilian populations, given the current sparse capabilities and inconsistent efforts to identify the agents of respiratory illness outbreaks. To address this need, the National Institutes of Allergy and Infectious Disease is

currently sponsoring a large, multi-center civilian adenovirus surveillance project (NIH grant number 1R01AI053034-01A2).

5.0 CONCLUSIONS

Diagnostic laboratory-supported surveillance efforts during the past half-decade reveal at least 14,750 febrile adenoviral respiratory illnesses among our young military recruits annually. This burden is shared by recruit training centers in all branches of the military. Tragically, up to ninety percent of these illnesses were preventable with previously developed vaccines. In contrast to historical studies, the current epidemiology of adenoviral FRI in recruits appears more closely associated with total population onboard (crowding) than winter season or cold ambient temperatures.

Reinstitution of the successful adenoviral vaccination program among our military recruits is badly needed, and a high priority of the current administration. A new manufacturer for the adenovirus vaccine was engaged in 2001. Safety and efficacy trials are currently under way in pursuit of Food and Drug Administration approvals by 2008 [60]. A description of the true burden of adenoviruses in the civilian community and a determination of the cost-effectiveness of adenovirus vaccines in civilians remain to be determined.

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DISCLAIMER

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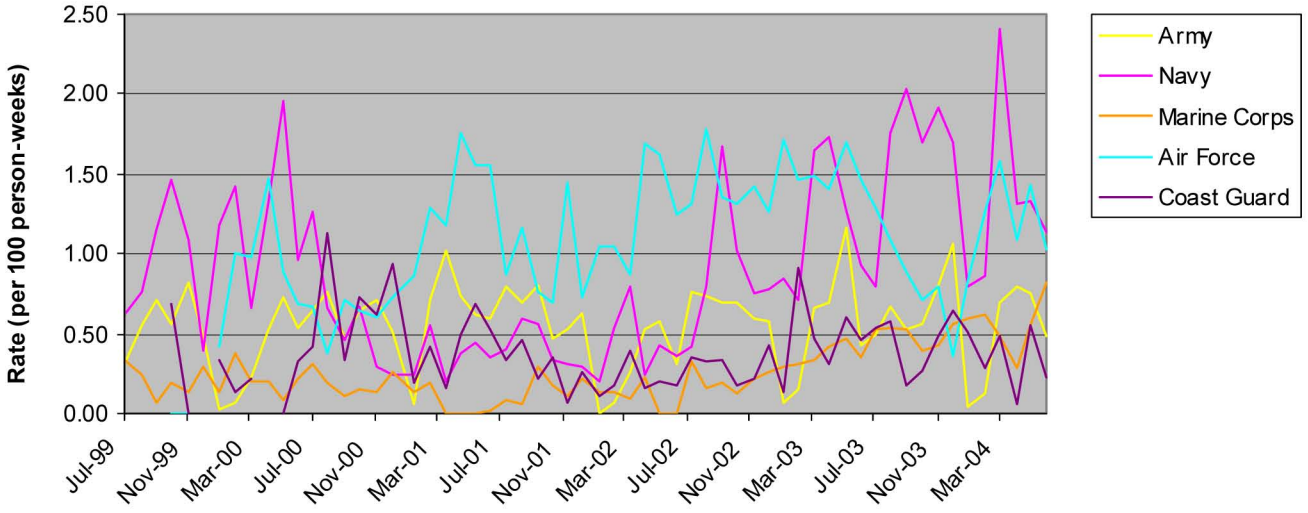

Figure 1. Estimated adenovirus infection rates by service, 1999-2004

Adenovirus infection rates by service (July 1999 to June 2004), as estimated by projecting the percentage of adenovirus positive among tested samples to the total counted febrile respiratory illness cases. Rates are expressed as number of cases per 100 recruit-weeks.

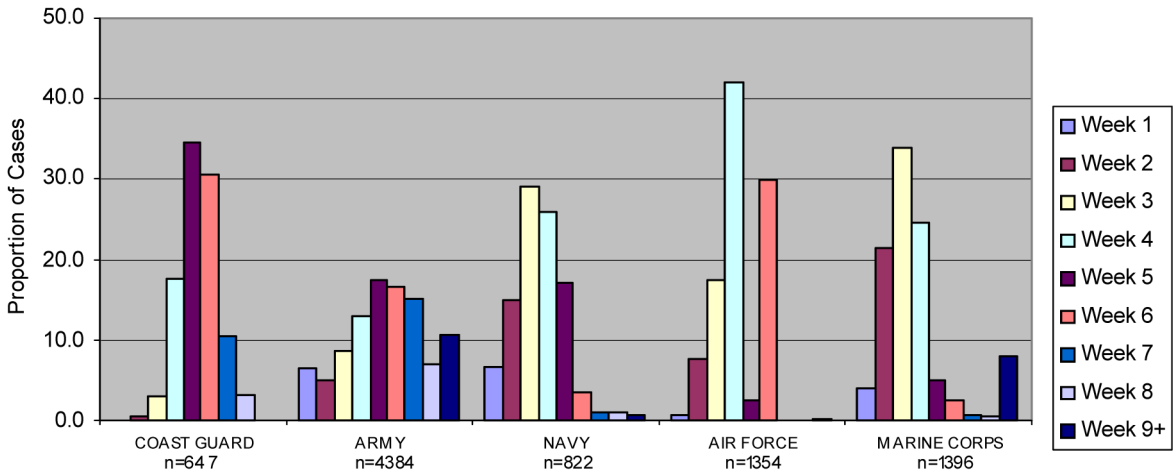

Figure 2. Proportion of adenovirus cases by week of training

Note that Marines have 12 weeks of training; therefore, week 9+ for the Marine Corps represents 4 weeks of person-time. During week 5, Air Force recruits are in the field, and capture difficult.

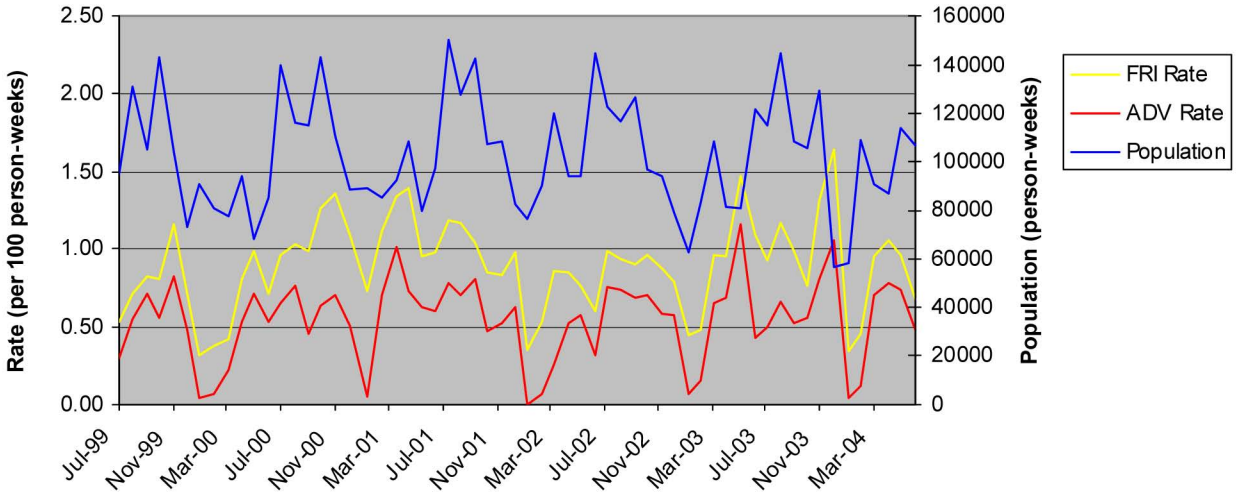

Figure 3. Army total febrile respiratory illness (FRI) and adenovirus (ADV)-specific FRI rates by total population onboard, 1999-2004

Graphic representation of the relationship between total recruit population onboard (blue line) with cases of FRI (yellow) and cases of adenoviral illness (red). As can be seen, when numbers of recruits being trained increase (crowding), rates of illness increase. The correlation coefficient between FRI rates and size of the populations in training was 0.263. Correlation between Ft. Jackson FRI rates and mean ambient temperature (not shown) at that site was 0.559.

Table 1

Febrile Respiratory Illness and Adenovirus-Associated Illness, Cumulative Data, July 1999–June 2004

Training Center	Total FRI Cases	Recruit-weeks	FRI Rate*	No. Specimens Collected	% Adenovirus Positive	Estimated No. Adenovirus Cases†
Army Fort Leonard Wood	14 355	1 619 864	0.89	2022	52.3	7742
Army Fort Jackson	23 122	2 617 350	0.88	3326	68.1	17 553
Army Fort Benning	18 687	1 916 087	0.98	2009	55.4	9169
Navy Great Lakes	28 237	2 359 105	1.20	1791	72.6	20 833
Marines San Diego	3 465	1 021 264	0.34	1053	74.4	2500
Marines Parris Island	4 274	989 053	0.43	999	71.8	2533
Air Force Lackland	17 101	1 268 259	1.35	1816	75.7	12 762
Coast Guard Cape May	931	187 103	0.50	867	76.4	656
Total	**110 172**	**11 978 085**	**0.92**	**13 883**	**66.8**	**73 748**

Abbreviation: FRI, febrile respiratory illness

*Cases per 100 recruit-weeks. The rates at each site are significantly different from each other ($p<0.0001$), with the exception of Fort Leonard Wood and Fort Jackson.

†Sum of monthly estimated cases over the 5-year period.

Table 2

Estimated Number of Adenovirus Cases by Training Center, July 1999-June 2004

	1999-2000			2000-2001			2001-2002			2002-2003			2003-2004		
Training Center	**Min Month**	**Max Month**	**Total**	**Min Month**	**Max Month**	**Total**	**Min Month**	**Max Month**	**Total**	**Min Month**	**Max Month**	**Total**	**Min Month**	**Max Month**	**Total**
Army Fort Leonard Wood	0	372	1353	7	265	1564	0	360	1231	0	334	1294	17	414	2300
Army Fort Jackson	5	629	3165	11	764	4068	2	482	3304	11	504	3023	2	759	3993
Army Fort Benning	4	230	923	31	391	2288	0	473	2118	24	480	2945	0	434	895
Navy Great Lakes	129	969	5700	65	790	2871	60	387	2214	151	884	3922	186	981	6125
Marines San Diego	7	107	440	5	80	321	5	54	257	21	72	608	0	130	874
Marines Parris Island	0	95	197	16	33	134	27	115	378	15	86	592	62	169	1233
Air Force Lackland	0	272	923	87	378	2422	151	339	2821	268	402	3926	62	332	2669
Coast Guard Cape May	0	35	60	3	41	212	3	16	102	4	24	158	1	19	124
Total			**12 761**			**13 880**			**12 426**			**16 467**			**18 214**
Yearly recruit-weeks			**2 265 252**			**2 453 357**			**2 626 424**			**2 315 712**			**2 317 340**
Adenovirus rate [*] (95% Confidence Intervals)			**0.56 (0.47-0.63)**			**0.57 (048-0.63)**			**0.47 (0.39-0.54)**			**0.71 (0.64-0.76)**			**0.79 (0.73-0.83)**

[*] Cases per 100 recruit-weeks. Rates were different throughout the years ($p<0.05$)

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14. ABSTRACT (maximum 200 words)

To determine the epidemiology of adenoviral illness among military recruits at eight military recruit training centers throughout the United States from 1999 to 2004, after loss of the adenovirus vaccines. Project staff at each site collected data from individuals with a febrile respiratory illness, and documented the total population at risk. Diagnostic samples were taken from a subset of the ill, and pathogen-specific rates were calculated.

Over the 5 years, nearly 12 million person-weeks were followed and an estimated 110 172 febrile respiratory illness cases and 73 748 adenovirus cases were identified. Rates of illness were highest at the Navy and Air Force training centers, with average annual rates of 1.20 and 1.35 cases per 100 recruit-weeks, respectively. Adenoviral-associated illness rates peaked in weeks 3 to 5 of training, depending upon service. The burden of adenoviral illness among US recruit populations has returned to pre-vaccination levels since loss of the vaccines. The annual cost of adenoviral illness was conservatively estimated at $21.52 million. Restoration of an effective adenovirus vaccine effort within the military is anticipated by 2008. Efforts to determine the burden of adenovirus and potential benefits of vaccination in civilian populations are being renewed

14. SUBJECT TERMS
adenoviral illness; military recruits, recruit training centers, adenovirus vaccines

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