THE WHITE HOUSE

WASHINGTON

February 5, 1996

MEMORANDUM FOR CAROL RASCO

FROM: Jennifer Klein and Debbie Fine

SUBJECT: FY95 DOD Bone Disease Research Funds

We met with several representatives of bone disease organizations a couple of weeks ago, along with staff from the Department of Defense. The outside organizations had requested the meeting in order to discuss their concern that $5 million appropriated in FY95 Defense appropriations bill has not yet been released by the Department.

The funds have been withheld because the Comptroller's office was not convinced that this research is "mission relevant;" the Health Division at DOD has made the case to the Comptroller that it is. In short, the Comptroller at Defense will release the funds if we recommend that they do so.

As far we can tell from our communications, the Health Division at DOD and Gordon Adams at OMB agree that funds ought to be released. We did not want to move forward on this without consulting with you.

We think that research in this area is relevant, as well as consistent with the Administration's priorities, and we therefore recommend that these funds be released. Do you agree with our recommendation?

_____ **YES** _____ **NO**

If you agree, we will make this recommendation to the Department of Defense.

Attached is a letter to Secretary Perry from 11 Senators in support of releasing the funds, along with some background information on the relevancy of bone disease research to the mission of DOD provided by the outside groups. We want to note that the letter to Secretary Perry has not yet been responded to -- DOD is waiting to hear from us.

Please let us know if you have any questions, or need additional information. Thank you.

United States Senate

SPECIAL COMMITTEE ON AGING
WASHINGTON, DC 20510-6400

December 8, 1995

The Honorable William Perry
Secretary of Defense
Department of Defense
The Pentagon
Washington, D.C. 20301

Dear Secretary Perry:

We are writing to express our support for the Department of Defense to initiate its research efforts on osteoporosis and bone related diseases funded by Congress in 1995. In the Fiscal Year 1995 Defense Appropriations legislation, funds totaling $5 million were appropriated for the Department of Defense to carry out osteoporosis and bone related disease research. Unfortunately, DOD continues to delay the release of these much needed funds.

Osteoporosis is a major health threat for 25 million Americans, 80 percent of whom are women. In the United States today, seven to eight million individuals already have the disease and 17 million more have low bone mass, placing them at increased risk for osteoporosis. Further, a great deal more research needs to be done in order to determine the causes of stress fractures in both servicemen and women.

We believe the need to expand present medical research on osteoporosis and bone related diseases is evident. Findings that emanate from such DOD efforts will not only assist our active duty forces but will also serve to find the means to treat the millions of Americans who are at high risk or have developed this debilitating disease. We ask that the funds already allocated by Congress be released so our military personnel can benefit from this much needed research.

In light of the 197,291 servicewomen in the Armed Forces and the trend toward more women entering the military, we strongly believe these diseases pose significant defense health risks and warrant the release of these important funds.

Thank you for your attention to this matter and please keep us informed of your efforts in this area.

Sincerely,

William S. Cohen

Daniel K. Akaka

Olympia J. Snowe

Dale Bumpers

Thomas A. Daschle

Bill Frist

Bill Bradley

Jesse Helms

Daniel K. Inouye

Carol Moseley-Braun

Tom Harkin

OSTEOPOROSIS AND DEFENSE

Osteoporosis affects 25 million Americans, 80 percent of whom are women. Each year there are 1.5 million osteoporotic bone fractures including more than 280,000 hip fractures, 500,000 vertebral fractures, 250,000 wrist fractures and the balance at other bone sites. The medical costs associated with this disease exceed $10 billion and are expected to dramatically increase as the population ages. Without intervention, the costs in the Year 2010 will exceed $60 billion and are expected to reach $240 billion by the Year 2050. Recently, the University of Southern California's Gerontology Center reported that the costs associated with osteoporosis and Alzheimer's disease threaten to swamp the medicare system.

Recently, we contacted the VA data center and found that, in 1993, there were more than 2,600 men over the age of 65 admitted to the VA hospital system due to hip fractures attributable to osteoporosis. These admissions accounted for 66,000 hospital care days. We have now requested information on the number of women who have received VA medical care for osteoporosis-related hip fractures. The average acute care cost of one hip fracture alone is $40,000. Since women are four times more likely to develop hip fractures, it is likely that the total number of admissions is much greater than the number cited above. It is unknown how many more men and women have received medical care for osteoporosis-related fractures of the spine, wrist and/or other bones.

Osteoporosis is essentially preventable and treatable; but, the disease must be prevented in 20 and 30 year olds. For once bone is lost, it cannot be replaced. Bone loss is progressive and irreversible: prevention is the key!

Presently, there are 197,291 servicewomen in the Armed Forces. This number represents 12.1 percent of the total active duty forces. As more women enter the armed services, osteoporosis will increasingly become a defense health issue. For many women, excessive physical training causes amenorrhea and leads to the loss of the protective effect of estrogen on bones. This bone loss eventually causes osteoporotic fractures. There is also evidence that males suffer activity-related hypogonadism, which may also lead to osteoporosis and fractures.

To address the problem, basic and clinical medical research is needed to:

- Overall, strengthen basic and clinical research programs to uncover the pathogenesis of osteoporosis, increase understanding of the basic cellular mechanisms by which bone remodeling is controlled
- Conduct studies on the pathogenesis and treatment of glucocorticoid-induced osteoporosis
- Study activity-related bone loss in women and men related to high-level physical activity
- Determine levels of activity which improve the skeleton, not impair bone metabolic function
- Study the parameters of short-term morbidity associated with musculoskeletal injuries related to training
- Study medical interventions which may offset bone loss in men and women
- Determine the etiology of hypogonadism in male recruits
- Determine which bone sites are most affected by physical training issues (excessive training usually causes low spinal bone mass, what happens at the hip?)
- Examine the level of musculoskeletal stress fractures due to equipment worn (boots) or carried during training

MILITARY MEDICINE. 157, 7:334, 1992

Factors Associated with Stress Fracture in Young Army Women: Indications for Further Research

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LTC Joseph R. Dettori, AMSC†

Several factors which affect bone density and predict risk of osteoporosis (e.g., ethnic origin, amenorrhea) are reportedly associated with a higher incidence of stress fracture in active premenopausal women. The authors surveyed 2,312 active duty Army women for the prevalence of ever having been diagnosed ("told by a doctor") with a stress fracture (16.1% of respondents) and examined the relationship between surveyable risk factors for low bone density and this self-reported stress fracture history (self-reported SF). Current smoking, previous history of amenorrhea (menses absent > 6 months), and known family history of osteoporosis were significantly associated with self-reported SF, while black ethnic origin was a protective factor. These data suggest hypotheses of stress fracture pathogenesis in Army women which bear further testing.

Introduction

Women in the United States now participate in exercise programs more than ever before. A subset of these women will develop stress fractures as a consequence of the increase in weight-bearing exercise.[1] Women are at substantially higher risk for stress fracture than men. This difference has been noted in military basic training, where 10–12% of women suffer stress fractures, compared to an incidence of 1–3% of men participating in the same training.[2–4] Bone remodeling is part of a normal response to physical stressors and this is generally expected to result in a stronger bone;[5,6] however, in some susceptible individuals, a debilitating fracture occurs in remodeled sites before the changes are complete.[4,7] Recent research attention has been focused on stress fracture in amenorrheic athletes, where menstrual status appears to play a role in determining which women will be most susceptible to stress fracture.[8] Presumably this risk is greater in individuals with lower bone densities and may also be related to other factors which predict risk of osteoporosis in women. These factors include Asian or white race,[9,10] family history of osteoporosis,[11] underweight,[12,13] exercise,[14] and factors related to a reduced estrogen level such as smoking,[15] episodes of amenorrhea,[16] and post-menopausal status.[17]

We conducted a pilot study to investigate the association of surveyable factors which have been linked to reduced bone density to self-reported history of medically diagnosed stress fracture (self-reported SF). This was performed with an Army population consisting primarily of premenopausal physically active women lacking significant illness.

Methods

A questionnaire was developed which asked 18 questions about the presence of factors associated with reduced bone density. The questions were brief and called for simple answers. An initial version of the questionnaire was administered to 50 soldiers who were then interviewed by a physical therapist (JRD) about their responses; the final form was a refinement based on this test survey.

We defined self-reported SF history as a positive response to the question: "Has a doctor ever told you that you had a stress fracture?" A few of these responses were reclassified as negative when the subsequent question ("If yes, what part of your body?") turned up improbable diagnosis more related to psychological stress, such as "brain" and "stomach." The types of stress fracture most likely to be detected and correctly diagnosed at a general medical treatment facility would generally be categorized as symptomatic, either with debilitating pain or frank fractures. Since medical records were not available in this anonymous survey, these self-reported SF cases could not be confirmed. In addition to misinterpretation of the diagnosis by some respondents, an unknown number of disorders may have been misclassified as stress fracture, including periostitis, compartment syndromes, infections, pre-existing bone problems (bone cysts, old injuries), or muscle fatigue problems.

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Thus, in this study we refer to these putative stress fracture diagnoses as self-reported SF with the understanding that these are unconfirmed diagnoses.

We defined amenorrhea as a 6-month absence of menses not associated with pregnancy. Family history of osteoporosis was indicated from "did your mother or your grandmother develop a hunched-over appearance or break their hips?", if this information was known. Weight trends were assessed by asking the women if they had ever exceeded Army weight standards (i.e., body mass index > 23–24 kg/m²) or if they had ever been told that they were underweight. Exercise habits were investigated by "how many days per week do you exercise?" and, since running is the primary form of organized exercise in the Army, we also asked "how many miles per week do you run?" The presence or absence of other factors were determined with simple "yes" or "no" questions.

The questionnaire was mailed to the duty addresses of every active duty female soldier at Fort Lewis, Washington in July 1987 (N = 2,462). The questionnaire was accompanied by a short letter signed by a female Army physician (JAN) soliciting participation in a study "important to the health of female soldiers." Soldiers were also asked to return separately an identifying postcard indicating whether or not they planned to return a survey form. Completed surveys were returned by 1,295 soldiers; 1,288 postcards were also returned, including 8 which indicated that the subjects would not participate. Four weeks after the first mailout, a second copy of the survey was sent to 1,092 soldiers who were presumed to have been reached by the first survey but had not returned a postcard. They were encouraged to return a survey if they had not already done so. A total of 1,630 out of 2,312 (70.5%) deliverable questionnaires were returned within 10 weeks of the first mailout and these were used in the analysis.

Factors associated with reported stress fractures were contrasted using a contingency table format with a chi-square test. Logistic regression was performed to determine the strength of the association between significant factors and stress fractures. The Mantel-Haenszel chi-square test was used to examine the effect of age and ethnic origin on the other factors (BMDP87, Los Angeles, California).

Results

The mean age in the survey sample was 26.1 ± 5.8 (SD) years (median age: 24 years; range: 18–52). The ethnic breakdown of respondents was 57.1% non-Hispanic white, 32.8% black, 5.0% Hispanic, 2.2% Asian, and 2.9% other or unspecified. In this sample, 16.1% of women had self-reported SF histories. The most prevalent location for the injury was the leg (53.2% of stress fractures reported) (Table I). Other known characteristics of the survey sample are presented in Table II.

Table II compares the percentages of women with self-reported SF in subpopulations of women with or without factors which affect bone density (chi-square test). Analysis by stepwise logistic regression yielded five factors independently associated with self-reported SF: history of amenorrhea, current cigarette smoking, non-black ethnic origin, known family history of osteoporosis, and young age. Age was included in the logistic analysis as a continuous variable and the skewed distribution was normalized with a log transformation. All of

TABLE I

LOCATION OF MEDICALLY DIAGNOSED STRESS FRACTURES

Location	Number	Proportion of all Stress Fractures (266)	Prevalence in Overall Sample (1,630)
Pelvis	15	5.6%	< 1.0%
Hip/thigh	23	8.7	1.4
Leg	140	53.2	8.6
Foot	74	28.1	4.5
Other	11	4.2	< 1.0
Total	263	99.9%*	16.1%

*Total is less than 100% due to rounding.

these terms and the likelihood ratio for the logistic model were significant at a probability level of 0.005 or less.

Based on the logistic analysis, the probability of self-reported SF ranged from 31.6% in a non-black smoker with episodes of amenorrhea and a family history of osteoporosis, down to 8.0% for a black non-smoker with normal menstrual history and a negative family history—a 4-fold difference. Relative risks (and 95% confidence interval) determined from the logistic analysis for amenorrhea, smoking, non-black ethnic origin, and family history were 1.36 (1.25–1.48), 1.32 (1.23–1.41), 1.28 (1.17–1.39), and 1.25 (1.16–1.35), respectively.

Age was a significant covariable for the prevalence of self-reported SF. Thus, from the logistic regression, older women with none of the four other risk factors would have a predicted prevalence as low as 1.5%. The actual prevalence in our sample for all women over age 40 (N = 42) was 1.4%, compared to the highest overall prevalences of 19.6% for women aged 22–23 (Fig. 1). This is a likely consequence of selective processes to this specific military population, as will be discussed. Dividing the sample roughly in half, at age 25, each of the other four factors was shown to be significantly affected by age (Mantel-Haenszel, $p < 0.001$). Odds ratios from the individual factor chi-square tables were similar to but slightly higher than those derived from the logistic analysis (Table III). Amenorrhea had a significant effect on stress fracture prevalence only in the younger women (29.9 vs. 16.0%, $p < 0.001$) compared to women > 25 years old (18.2 vs. 12.7%, $p = 0.12$). Age was also a significant cofactor for underweight, with only the younger women demonstrating a significant relationship between self-reported SF and being underweight ($p < 0.05$; Mantel-Haenszel test, $p < 0.05$). Other factors such as parity and use of oral contraceptives were age-related (Fig. 2) but had no association with prevalence of self-reported SF.

Black women were significantly more likely to have had children (51.5 vs. 36.8%; $p < 0.001$), were more likely to use oral contraceptives (40.9 vs. 31.6%; $p < 0.001$), and were less likely to be current smokers (32.1 vs. 37.8%; $p < 0.001$), all factors which have been reported to be protective against stress fracture or osteoporosis. Only 12.0% of black women reported a family history of osteoporosis, compared to 38.2% of non-black women. Nevertheless, a positive family history of osteoporosis was associated with a 10% higher prevalence of self-reported SF, with no difference between blacks and non-blacks (p = 0.62). Ethnic differences in stress fracture were apparent only when family history of osteoporosis was negative ($p < 0.01$; Mantel-Haenszel chi-square test, $p < 0.01$).

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TABLE II

PREVALENCE OF STRESS FRACTURE IN ASSOCIATION WITH SURVEYED FACTORS RANKED IN ORDER OF FACTOR PREVALENCE IN THE SAMPLE

Factor	% of Total with Factor	% with History of Stress Fracture		
		Factor Present	Factor Absent	
Ethnic origin (white or Asian)	87.3	18.5	11.3	***
Nulliparity	58.4	16.1	16.2	
Gynecological age ≤ 20 (1)	(16.6)	19.3	14.5	
More than 2 births (1)	(12.7)	15.4	17.0	
Age (≤ 25 years)	44.8	18.2	13.6	**
Cigarette smoking (ever)	55.1	19.4	12.0	***
Cigarette smoking (current)	34.6	21.9	13.1	***
Have smoked for > 10 years (2)	(30.4)	24.8	20.4	
More than one pack/day (2)	(19.2)	24.6	20.7	
Current oral contraceptive pill use	34.6	17.6	15.1	
Ever on the Army Weight Control Program (BMI > 23–24 kg/m²)	31.0	16.9	15.7	
Family history of osteoporosis	29.8	21.8	13.5	***
Running exercise (> 10 miles/week)	21.0	19.0	15.4	
Ever told that they were underweight	16.9	20.5	15.4	*
History of amenorrhea (episodes of ≥ 6 months)	14.9	22.7	13.4	***
Late menarche (> 16 years old)	3.6	19.0	18.1	

Notes: chi-square test: significance: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
Subsamples: (1) parous women ($n = 698$); (2) current smokers ($n = 581$).

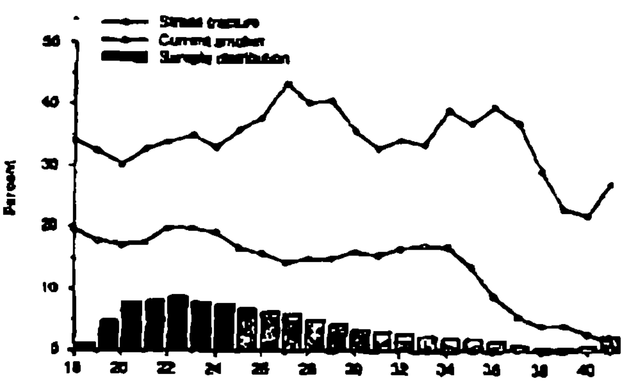

Fig. 1. Distribution of respondents by age (bars) and the prevalence of self-reported SF and current smoking. The line graph data are expressed as a three-point running mean.

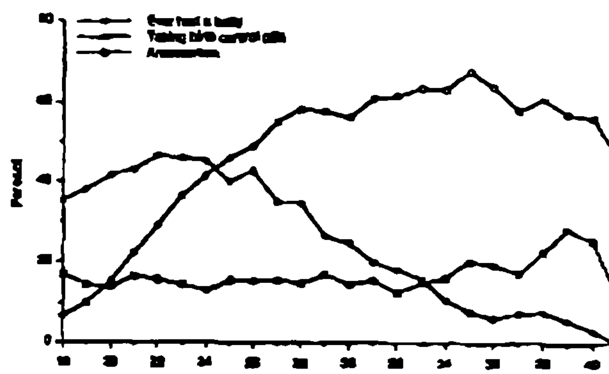

Fig. 2. Prevalence of parity, oral contraceptive use, and menstrual irregularity by age in active duty Army women. Data are expressed as a three-point running mean.

TABLE III

ODDS RATIOS OF FACTORS ASSOCIATED WITH STRESS FRACTURE STRATIFIED BY AGE

Factor	Age Group	Odds Ratio	Probability	Pooled Odds Ratio (95% Confidence Interval)
Amenorrhea history	≤25	2.24	0.0002	1.93 (1.37–2.72)
	>25	1.53	0.12	
Current smoker	≤25	1.96	0.0001	1.91 (1.45–2.51)
	>25	1.84	0.005	
Ethnic origin (white/Asian)	≤25	1.78	0.003	1.82 (1.33–2.50)
	>25	1.94	0.02	
Family history	≤25	1.68	0.01	1.88 (1.38–2.55)
	>25	2.22	0.0007	

A positive history of amenorrhea eliminated the relation between smoking and stress fracture, with more stress fractures in smoking vs. non-smoking women without history of amenorrhea (20.3 vs. 11.6%, $p < 0.001$) but with no differences between smoking and non-smoking women with a history of amenorrhea (28.6 vs. 21.8%, $p = 0.23$) (Mantel-Haenszel test, $p < 0.001$). Smoking had a comparable effect on the relation between amenorrhea and self-reported SF, with a significant relation in non-smokers ($p < 0.001$) but not in smokers ($p = 0.08$) (Mantel-Haenszel test, $p < 0.001$). More women had experienced episodes of amenorrhea in the subpopulations of women who had (ever) been told that they were underweight (23.7 vs. 13.2%) and who were runners (> 10 miles/week) (20.3 vs. 13.4%, $p < 0.05$).

Discussion

The prevalence of self-reported SF in the women in this survey (16.1%) is consistent with other reports. Eleven percent of the women surveyed had both a history of stress fracture and reported that during basic training they had bone pain which was sufficiently debilitating that they had to stop running. Although we did not specifically ask if stress fracture was diagnosed in basic training, it is probable that many of the self-reported SFs occurred in basic training, at a rate which is comparable to the 10.5% observed in a group of 114 female Marine recruits during basic training,[18] 10.0% observed in the first 8-week training period at the U.S. Military Academy,[3] and 11.3% observed in 186 Army recruits in basic training.[4] Assuming in the worst case that all of our nonrespondents were disinterested women with no history of stress fracture, we would still have a self-reported SF prevalence of greater than 10%.

Most previous studies of stress fracture have been conducted with elite athletes and little is known about risks to the general population. Although our sample is skewed toward younger women and it excludes individuals with conditions which significantly affect physical performance since this is a condition of continued Army employment, this study yields information about healthy young women who are otherwise typical of the general U.S. population. Generalization about older active women must be made with caution because of the selective processes which determine their presence in this sample, and because the intensity of physical training for women during Army basic training (where stress fractures tend to emerge) increased markedly in 1978.

The association of smoking with self-reported SF is one of the most interesting findings to emerge from this study. Cigarette smoking has been associated with reduced bone mineral content and osteoporosis,[15,19] although some studies have failed to demonstrate a connection.[20] Our results provide the first suggestion of such a relationship to stress fractures, in a population which is almost entirely premenopausal. Smoking reduces serum estrogen levels in a dose-related relationship, possibly through a nicotine-induced increase in hepatic metabolism,[21,22] and this reduction in estrogen levels has been linked with a trend to reduced bone mineral density in smokers.[22] It may also be important that our smokers had a higher prevalence of self-reported SF than women who were former smokers since this suggests that smoking may be a modifiable risk factor. We did not find any additional differences in self-reported SF between duration of smoking (analyzed as a continuous variable; data not shown) or smoking more than one pack per day in the current smokers.

Amenorrhea is also a factor identified in this study which may be modifiable through physician intervention. Our data confirm previous findings in collegiate women athletes, where stress fractures were observed in 24% of women with irregular or absent menses but in only 9% of the women with normal menses.[6] Like smoking, the effect on bone is presumably produced by episodes of hypoestrogenism.[16,23,24] Indeed, women with a history of amenorrhea did not have a significantly higher prevalence of self-reported SF if they also smoked, nor was there a significant association between amenorrhea and self-reported SF in women who smoke, suggesting a single mechanism by which these two factors may produce a marked susceptibility to self-reported SF. This effect on bone density appears to be reversible with a resumption of menses.[25] The data suggest that amenorrhea is a symptom which may signal higher risk of bone injuries in women engaged in vigorous weight-bearing activities, such as running or marching, and measures should be taken to return such individuals to normal menstrual patterns. Protective measures might include reduced training volume or the prescription of estrogens (with opposing progestagens) by a physician if a significant reduction in bone density is established.

Lloyd et al.[6] found that risk of stress fracture was lower in those who used oral contraceptives. We did not find any significant relation to the use of oral contraceptives, but this may be related to the difference in prevalence of amenorrhea in our study population. The prevalence of amenorrhea may be high in some athletes and, in these women, the low-dose estrogen of many contraceptive preparations may offer some protection against bone loss. In contrast to athlete samples, only 14.9% of our population reported amenorrhea "ever" and only 1.3% of the non-pregnant women in our sample were currently amenorrheic (>6 months since last menses at the time of survey); 10% of our respondents were currently pregnant. This rate of amenorrhea is similar to the point prevalence rate of 1.8% reported in a Swedish survey of a normal community.[26]

In our study, women running over 10 miles/week or having been told they were underweight were also more likely to have a history of amenorrhea, but these factors appear to be only loosely associated. Exercise serves as the stimulus for bone remodeling but whether this will result in an increase in bone density or in a stress fracture appears to be dependent on other factors, such as history of amenorrhea. This is suggested by our data, and by the results of studies of female athletes where the rates of stress fracture in eumenorrheic exercising women were unremarkable.[6] Intense exercise may be involved in amenorrhea, as evidenced by the return of menses in some amenorrheic women who reduce their exercise,[27] but amenorrhea is not a necessary consequence of intense exercise.[28] Similarly, low weight (or low body fat) does not necessarily produce amenorrhea.[29] These three factors may be non-causally associated as common aspects of a behavioral and/or hypothalamic disorder.[30] Underweight was associated with an increased likelihood of self-reported SF in the younger women (<25 years old) but, although body weight is a factor in bone mass,[31,32] underweight did not emerge as an independent factor associated with self-reported SF in this study.

Positive family history is recognized as a risk factor in osteoporosis,[11] and a reduced bone mass has been demonstrated in relatives of osteoporotic patients.[33] Family history was a factor associated with an increased prevalence of self-reported SF in both black and non-black women in our study. Ethnic origin was a second unrelated hereditary factor associated with self-reported SF. The reduced risk of osteoporosis in black women is associated with a greater bone density, perhaps as a result of reduced osteoclast activity.[34] Whether or not this reduced excavation of bone persists during an exercise-induced remodeling remains to be demonstrated, but the achievement of a higher bone mineral density in black women is of itself likely to be protective of stress fracture, an association confirmed in this study. Brudvig et al.[35] found that the 1-year incidence of stress fracture was 1.4 in black women compared to 11.8 in white women in a young population of basic recruits reporting to a physical therapy clinic. While the incidence was lower in males, there was still a lower incidence in black males than white males. Our data confirm this protective effect of black ethnicity on stress fracture.

This study suggests hypotheses for further investigation, specifically the possibility that smoking, amenorrhea, and family history of osteoporosis are risk factors for stress fracture in young women, while black ethnic origin may be a protective factor.

Acknowledgments

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Riley, KS, reduced costs of inpatient psychiatric and residential care from $3,900,000 in fiscal year 1991 to $870,000 in fiscal year 1994, a savings of $3,030,000 with good long-term treatment effectiveness. With the Department of Defense spending 80 percent of its CHAMPUS residential treatment care dollars on 20 percent of the RTC population, recidivism must be addressed.

The Committee, therefore, directs the Department to implement a program of residential treatment services which incorporates wraparound services as part of such care for military beneficiaries in TRICARE regions 7 and 8.

Psychology Demonstration Program.—The Committee supports the continuation of this program with representation from each service and requests that the Department provide the results and recommendations of that program to the Committee no later than September 30, 1996.

Information network.—The Committee believes there is a need for development of a high-speed health care information, education, and data gathering network. The Committee directs that funds should be provided to enhance network infrastructure as well as test new delivery technologies that can improve organization and access to critical data and expand applications in the field.

Disaster management training.—The Committee endorses efforts by the Tripler Army Medical Center to pursue the development of a joint Department of Defense and University of Hawaii Center of Excellence in disaster management training, research, technology, and logistics. The Committee encourages Tripler Army Medical Center to use available budget resources to continue these programs.

Incentive special pay [ISP].—The Committee directs that the Assistant Secretary of Defense for Health Affairs review the Department's policy for the disbursement of incentive special pay to ensure that all ISP's are paid consistently.

Neurofibromatosis [NF].—From within funds available under this heading, the Committee urges the Department to provide not less than $8,000,000 in financial and technical support toward the study of neurofibromatosis.

Nonequity in rank structure.—The Committee reiterates its position that general officer selection and development programs in the health care field should be based on fair and equitable criteria.

Paget's disease.—Of the available funds, the Committee urges the Department to provide not less than $1,000,000 in financial and technical support toward the study of Paget's and related bone diseases.

Comprehensive health care system.—The Committee notes that in March 1995, the Department awarded a multiple-vendor D/SIDDOMS contract in support of the comprehensive health care system [CHCS] project. This contract is meant to provide products and services to maintain and expand automation in military hospitals when the current CHCS contract expires in early 1996. The Committee encourages the Department to continue the development of CHCS in the spirit of open competition and to ensure the utilization of commercial-off-the-shelf [COTS] products in accordance with existing requirements.

pose. And, as the Department's managed care support program evolves, new and creative means must be established to identify and implement advancements in health care delivery systems.

Recognizing this, the conferees agree with the Senate proposal to establish a military health care advisory council or forum. This body should serve as a unique mechanism for transmitting ideas, identifying problems, and/or developing regularized and productive communications between the military health services system, the private sector, and other interested third parties.

At a minimum, this body should incorporate the following principles:

A representation scheme which guarantees both equal opportunity for all interested parties and a diverse mix of participants.

An advisory function only—one that has no part to play in the technical procurement structure—so as to minimize both the perception and the reality of influencing the contractor selection process.

The conferees are willing to provide the Department of Defense with considerable discretion as it goes about meeting the intent of the Congress with respect to this matter. But, in no case, will the conferees accept unreasonable delay or stonewalling by the Department in the implementation of this program. Thus, the conferees look forward to working with the Department of Defense and, in particular, the Assistant Secretary of Defense for Health Affairs to determine the exact details of this advisory body over the coming months.

CLEFT LIP AND PALATE SURGERY

The conferees endorse the U.S. government program which provides cleft lip and palate surgery for children in Honduras. The conferees agree that necessary travel expenses incurred by military doctors should be paid from within the program funds as in the past.

MEDICAL RESEARCH

The conferees recommend a number of adjustments to medical research and development. The table below highlights those medical program elements to which there has been an adjustment.

Research, development, test and evaluation

[In thousands of dollars]

P.E. title, and program	*Conf.*
Army:	
0601102A—Def. Res. Sciences:	
Trauma Care	150
Nutrition	250
Serum Cholesterol	425
0602787A—Medical Technology:	
Nutrition	750
Tissue Rep.	5,000
Dengue Fever	1,000
Epidermolysis Bullosa	1,000
0603002A—Medical Adv. Tech.:	
Breast Cancer	150,000
Prostate Cancer	4,250
Women's Health	40,000
Ovarian Cancer	7,500
Cell Regulation	2,000
Mammography	2,000
Spinal/Brain Res.	0
Lyme Disease	600
Coastal Cancer Control Program	5,000
Osteoporosis	5,000
Nutrition	750
0603105A—AIDS: AIDS Research	33,410
0605898A—Management Headquarters (Research and Development): Akamai	12,000
Navy:	
0603216N—Aviation Surv: Naval Biodynamics Lab.	700
0603706N—Medical Dev:	
Naval Biodynamics Lab.	700
Bone Marrow	34,000
Mammography Dev.	2,000
Breast Cancer Center	5,000
Defense-wide:	
0603706D—Cooperative DOD/VA Cooperative Research:	
General Research	20,000
Spinal/Brain Res.	15,000
Prostate Cancer	10,000
Gulf War Syndrome	5,000
Total	363,385

MEDICAL ADVANCED TECHNOLOGY

The conferees have provided $150,000,000 to continue the Army's breast cancer research program. The conferees have allocated $20,000,000 for mammography efforts as approved by the House. The conferees are aware of a new application of military technology, relying on optical correlators, which can enable automated mammography screening. The conferees urge the Army to consider such applications of military technology within this program.

A portion of the increase, $15,000,000, is provided for institutions with dedicated breast cancer centers as described in House Report 103-254 which accompanied the Department of Defense Appropriations Act, 1994. The remaining funds shall be used to continue ongoing and initiate new breast cancer research under a solicitation developed by the Department of the Army in conjunction with a Breast Cancer Research Program Integration Panel similar to the fiscal year (FY) 1993 panel process. The conferees urge the Army and the panels to solicit research proposals in the Institute of Medicine (IOM) strategy that were not well represented in the FY 1993 DOD program.

COASTAL CANCER CONTROL PROGRAM

The conferees provide $5,000,000 to the Charleston Naval Hospital only to support the development and implementation of a Coastal Cancer Control Program in conjunction with a State-owned comprehensive cancer center serving coastal South Carolina. The conferees recognize that upon the closure of the Myrtle Beach Air Force Base and the Charleston Naval facilities, access to critical preventive health care services for military dependents along coastal South Carolina has become more difficult. The Coastal Cancer Control program will address this reduced access to care and resulting increased cancer mortality by providing mobile screening, education, preventive intervention, and follow-up care to military dependents and other medically underserved citizens of coastal South Carolina.

OSTEOPOROSIS RESEARCH

The conferees agree to provide $5,000,000 for research into osteoporosis and related bone diseases. This work should be done in close coordination with the National Institute for Arthritis and Musculoskeletal and Skin Diseases, the lead institute for bone disease research.

TEAM COORDINATION IN EMERGENCY MEDICINE

The conferees support The Army research transferring lessons learned from aviation crew coordination training to emergency medicine. This research will reduce patient risk and increase efficiency through improved hospital emergency care. The conferees direct that funds be made available within the Medical Advanced Technology program (PE 603002A) for the demonstration of this program at Madigan Army Medical Center by the Army Research Lab in coordination with Rhode Island Hospital. The conferees encourage the Department of Defense to consider deploying this program at all of its military treatment facilities.

BRAIN AND SPINE RESEARCH

The conferees agree to provide $15,000,000 in Cooperative DOD/VA Medical Research funding only for the continuation of the DOD Military Medical Personnel Collaborative Spinal Cord Injury, Paralysis, Neuroscience Research, Education and Training program initiated in 1992.

TRANSURETHRAL HYPERTHERMIA

The conferees are aware of the promising preliminary results of work being done to develop prostate treatments which do not require surgery. However, it is necessary to conduct randomized trials to more clearly understand the benefits of non-surgical procedures such as transurethral hyperthermia. Therefore, the conferees direct the Department to use a portion of this funding to finance a well defined scientific study comparing the surgical treatment for benign prostatic hyperplasia with hyperthermia. The multi-year trial shall be conducted at a university medical center with a National Medical Technology Test Bed affiliated with a veterans hospital in California.

GULF WAR SYNDROME

The conferees have provided $5,000,000 within the Cooperative DoD/VA Medical Research program element for competitively-awarded independent research on Gulf War Syndrome.

Amendment No. 113: Deletes a House provision making a portion of the appropriation subject to authorizing legislation. Adds Senate language providing for nursing research and communications services for members of the Armed Forces from the American Red Cross. Amends Senate language regarding the Plattsburgh AFB Hospital.

CHEMICAL AGENTS AND MUNITIONS DESTRUCTION, DEFENSE

Amendment No. 114: Appropriates a total of $575,449,000 for Chemical Agents and Munitions Destruction, Defense instead of $562,949,000 as proposed by the House and $590,149,000 as proposed by the Senate.

OPERATION AND MAINTENANCE

Amendment No. 115: Earmarks $355,784,000 for operation and maintenance instead of $345,784,000 as proposed by the House and $363,584,000 as proposed by the Senate. The conference agreement includes the following specific increases above the budget:

Outreach	$2,000,000
Risk Analysis	3,000,000
Surveillance	4,600,000
JACADS Storm Recovery	10,000,000

The conference agreement also incorporates the three specific reductions, totaling $19,300,000, included in the House bill.

PROCUREMENT

Amendment No. 116: Earmarks $196,965,000 for procurement instead of $196,465,000 as proposed by the House and $215,265,000 as proposed by the Senate. The conference agreement includes the following increases and decreases from the budget:

Activated Carbon Filters:	
Equipment Modification Design	+$9,200,000
Tooele facility	+18,200,000
Anniston facility	+15,000,000
Umatilla facility	+20,600,000
Equipment, Pueblo facility	−24,700,000
Equipment, Pine Bluff facility	−32,300,000
Equipment, Umatilla facility	−15,700,000

RESEARCH, DEVELOPMENT, TEST AND EVALUATION

Amendment No. 117: Earmarks $20,700,000 for research, development, test and evaluation as proposed by the House instead of $11,300,000 as proposed by the Senate.

FY 95 APPROPRIATIONS

NATIONAL OSTEOPOROSIS FOUNDATION

December 7, 1995

Joseph Osterman, Ph.D.
Director
Environment and Life Sciences
Room 3D 129
Pentagon
Washington, D.C. 20301

Dear Dr. Osterman:

As the President of the National Osteoporosis Foundation (NOF), I am writing in response to your finding that osteoporosis has no relevancy to military personnel. It is my understanding that, as a result of your finding, the Department of Defense (DOD) will reject the $5 million line item for osteoporosis research included in the DOD FY 1995 Appropriations Act. I appreciate the opportunity to respond to your finding, and I hope that the additional information contained in this letter regarding the impact osteoporosis may have on military personnel will assist you in reconsidering your position on this important issue.

Osteoporosis is a major public health threat to 25 million individuals -- 80% of whom are women. In the U.S. today, 7-8 million Americans already have the disease and 17 million more are at risk due to lower-than-normal bone mass. Each year the disease causes an estimated 1.5 million fractures, including hip, vertebral, wrist and other fractures. The medical costs associated with this disease nationwide exceed $10 billion annually -- a figure that is expected to increase dramatically as the population ages.

Despite these staggering figures, osteoporosis is preventable if measures are taken before an individual reaches the mid-30s -- which encompasses the time period that many men and women spend in the military. Skeletal development in average healthy individuals is maximal at age 25 in women and age 30 to 35 in men. Once bone is lost, it can never be fully replaced, so prevention is of the utmost importance. It is tragic that relatively little is known about the impact of exercise and calcium intake on building peak bone density of young people as a preventive measure. It is essential that our youth in the military build up their bone mass to maximum capacity in order to be well equipped throughout their life span.

There are many factors that support the need for osteoporosis research in the military:

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• Fax 312/464-5830

1. Institute of Medicine recommendations

- A recent report by the Institute of Medicine recommended a long-term Defense Department commitment to, among other topics, longitudinal studies on the risk factors of osteoporosis and measures for its prevention (IOM, 1995, p. 37). The report also stated that there is a need to examine the prevalence of menstual dysfunction and subsequent health concerns such as stress fractures and osteoporosis (p.43).

2. Increased number of women in the military

- There are approximately 340,000 women in the US Armed Forces, nearly 200,000 on active duty and 140,000 in the reserve (ibid.). Women now comprise 14% of the total military active-duty force, including 12.8% of all officers. Some recruiting projections suggest this number may rise to 20% in the near future (Gunby, 1995). With the increasing number of women in the military, the health conditions of this population will become increasingly important if they are to serve at maximum capacity and strength, especially through the training process, the most expensive part of military life.

3. Strenuous training can cause bone loss in women and men

- Strenuous physical exercise induces amenorrhea, the cessation of menstruation, which can cause bone loss that may lead to stress fractures. Amenorrhea occurs at a higher rate in women who engage in strenuous physical exercise. I have cited a number of studies in the bibliography that support this point. But I would like to highlight one particular study of 2,312 active-duty Army women with self-reported stress fractures (16.1%). This number reveals a positive relationship between stress fractures and known risk factors for osteoporosis such as smoking, previous history of amenorrhea, and known family history of osteoporosis. The authors of this study concluded that the data suggest hypotheses of stress fracture pathogenesis in Army women that bear further testing (Friedl et al., 1992).

- Another study found that 55% of trainees in a light infantry unit suffered a training-related injury, with stress fractures accounting for the largest number of limited duty days. The authors (Reynolds, et al., 1994) concluded that cigarette smoking and low endurance levels were risk factors. But, one must wonder how many of the women with stress fractures had a history of amenorrhea? A medical history of amenorrhea could, with further study, perhaps be added as a screening device when selecting new recruits.

- In a four-year study of soldiers in basic training, 1,338 stress fractures were confirmed in a population of 109,000 (Pester, et al., 1992). Female soldiers suffered more than twice the number of bilateral fractures as the male soldiers, and 1.09% of the women compared to .09% of the men experienced any fractures. Modifications were implemented that resulted in significantly fewer fractures in the men (16.19% decrease) and less in the women (7.32% decrease). Why did the modifications have a more dramatic effect on the men than on the women? The issue of bone density could certainly have played a part in these fracture rates. Since women in the military are at substantially higher risk for stress fracture than men, these findings should be of significant concern to the military.

- In an unpublished study in which male and female West Point cadets were followed over a four-year period and tested every six months, bone density dropped during the first year of service. The loss was greatest during the first six months when the cadets partook in the most strenuous exercise. The authors hypothesize that exercise-induced injury is associated with decreased bone density. This calls for considerable more study. First, it would be extremely valuable to follow these cadets through their military careers. Second, one might also look at the correlation between birth control pills, bone density, and injury rates in females. A third possible study might involve the relationship between low free testosterone levels and injury rates (Copley, Lindberg, et al., unpublished).

- Would varying daily activity involved in the basic training program lower stress fracture rates? It has been suggested that doing the same exercises every day is unhealthy. Dr. Snow's research in her longitudinal study of elite female runners (mean age of 21) indicated a significant decline in bone density over an eight-month period. The decrease occurred in amenorrheic as well as in eumenorrheic runners. She theorized that the bone remodeling cycle is altered in favor of resorption due to insufficient recovery time. These women rarely took a day off from running -- similar to basic training of female recruits (Snow et al., 1995).

4. Eating disorders in women can cause bone loss

- Women also become amenorrheic from eating disorders. Subjects with anorexia nervosa have demonstrated decreased rates of bone formation and an increased rate of bone resorption (Abrams, et al., 1993). Low bone mass seems to persist following recovery, indicating that bone mass deficits acquired in adolescence may not be completely reversible (Bachrach, et al., 1991). The onset of anorexia nervosa before attainment of peak bone mass and prolonged duration of amenorrhea result in the most significant loss of bone mass (Biller, et al., 1989; and Hay, et al., 1992).

Approximately 1-4% of young women in the U.S. currently suffer from anorexia nervosa or related disorders, and it is quite possible that a similar percentage exists in the military. There is currently no information about eating disorders, amenorrhea and military women.

- There also is no information regarding young African American women who suffer from amenorrhea or eating disorders. African American women tend to have lower rates of osteoporosis due to a genetic tendency toward denser bone mass; however, very little is known about this population's physiology in relation to bone resorption and formation. A high percentage of women in the military are African American and such information could be extremely important as this minority population increases.

5. Smoking can cause bone loss

- Another risk factor associated with bone loss is smoking (Waldholz, 1994). While smoking is banned at most Defense Department work sites, 31% of women on active duty are smokers (Gunby, 1995), a percentage slightly higher than the national average of 25%. However, bone loss due to smoking in not limited to women; smoking also lowers bone density in men (Slemenda, et al., Annals of Internal Medicine 1992). Smoking in the military could result in an increased financial burden when caring for military retirees in the future; therefore, research into links between smoking and osteoporosis that could then be used in smoking cessation programs could be of great value.

6. Quantitative ultrasound can predict stress fracture risk in female army recruits

- The new methods of measuring bone density now available, such as dual energy x-ray absorptiometry, bone markers, and ultrasound would allow the military to screen military recruits for low bone mass. DOD-sponsored research -- currently only available as an abstract -- finds that ultrasound can predict stress fracture risk in female army recruits. A recruit with broadband ultrasound attenuation (BUA) of 63 has a 1-in-8 chance of having a stress fracture during basic training (Kimmel, D.F. et al., 1995). A quantitative ultrasound thus predicts stress fracture risk during basic training in women. This same instrument can also identify persons with high bone strength. Individuals with high bone strength would be well-suited for especially physically demanding duty such as paratroopers, Rangers and the like.

6. Dietary calcium intake can build bone mass

- While protecting "bone health" in young people can be a problem, there are studies that clearly indicate the benefits of addressing this problem. For example, one study of calcium supplementation in adolescent girls resulted in significant increases in total body and spinal bone density (Lloyd, et al., 1993). Another study of adult women in China from five rural areas where dietary calcium varied considerably concluded that daily increases in dietary calcium significantly increased bone mass (Ji-Fan HU et al., 1993). With further research, the military could assure that its recruits increased their daily intake of calcium, thus ensuring their future bone health.

In summary, I hope you will agree that we have presented a compelling case which will cause you to reconsider the relevancy of osteoporosis to the military. As you know, the Military Health Services System serves 8.3 million people, including active and retired military personnel and their dependents. In FY95, program costs were about $15.3 billion. To contain health costs, prevention is key, and research is the first step in prevention. The increasing number of women in the military presents new health challenges, some of which are directly related to osteoporosis. Understanding the correlation between bone loss and excessive exercise, amenorrhea, and smoking in military personnel will only serve to strengthen the overall readiness of the defense system as well as generate significant cost savings through reduction of stress fractures. It also will save health care dollars by preventing costly fractures in the aged.

The $5 million appropriated to the DOD in FY 1995 could fund important research projects that seek to answer some of the many questions remaining about bone loss in the second, third and fourth decades of life. With the new methods of measuring bone density, the military has an excellent opportunity to study the determinants of peak bone mass and early bone loss.

The National Osteoporosis Foundation remains at your service to assist you with any questions this letter may have raised. Please contact me at (914) 947-3000 (x3494), or Bente E. Cooney, Director of Public Policy at (202) 223-2226.

Sincerely,

Robert Lindsay, M.D., Ph.D.
President
National Osteoporosis Foundation

ANNOTATED BIBLIOGRAPHY
OSTEOPOROSIS AND THE MILITARY
(in descending chronological order by topic)

RECOMMENDATIONS FROM INSTITUTE OF MEDICINE

Recommendations for Research on the Health of Military Women. Committee on Defense Women's Health Research. *Institute of Medicine.* National Academy Press, Washington, DC 1995.

The committee recommends that the research problems or questions to be studied are unique to military women (e.g., a study of the potential reproductive toxicity of chemical weapons or medications used to counter them), or is especially prevalent among military women (e.g. a study of rapid diagnosis and treatment of sexually transmitted disease, or of stress fractures and other overuse injuries common in basic training, or is related to the ability of military women to perform their mission responsibilities (e.g., a study of the effect of premilitary abuse on response to violence and trauma).

INCREASING NUMBER OF WOMEN IN THE MILITARY

Unique Medical Problems of Military Become Part of Intensified Research into Women's Health. Phil Gunby. *Journal of the American Medical Association.* September 27, 1995; 274(12) :932-933.

A report from the Committee on Defense Women's Health Research recommending long-term Defense Department commitment to longitudinal studies on questions of the aging process and physical skills required in the military, risk factors for osteoporosis, relationship of joint disease and physical activity, occupational exposures and cancer risk, and psychiatric sequelae such as posttrauma disorder. The committee added that a focus for further research should be on military women's physiological, psychological, nutritional, and behavioral response to a number of factors in military life.

Exercise, Age and Bones. Thomas WC Jr. *Southern Medical Journal* 1994 May; 87(5) :S23-5.

Skeletal development in average healthy individuals is maximal at age 25 in women and at age 30 to 35 in men. The degree of osteopenia in the elderly depends partly on skeletal development during formative years and can be prevented from becoming severe by maintaining good nutritional status and physical activity. Maintenance or actual increase in muscle mass is a desired effect of appropriate physical activity, but excessive physical exercise may induce estrogen deficiency and menstrual irregularities in premenopausal women.

THE IMPACT OF EXCESSIVE EXERCISE ON BONE DENSITY IN WOMEN

Bone Health and Prevention of Osteoporosis in Active and Athletic Women. Snow-Harter CM. *Clinical Sports Medicine* 1994 April; 13(2) :389-404.

> To prevent both stress fractures and premature osteoporosis, active and athletic women should be encouraged to keep accurate records of their menstrual cycles and monitor any divergence from normal with bone mass evaluation. Recommendations for treatment include decreased training and volume, increased calcium intake, increased resistance training and possibly estrogen replacement therapy for those who are not willing to make changes in diet and exercise level.

Lumbar Spine and Hip Bone Mass Changes in Female Runners and Gymnasts. Robinson, TL, Snow-Harter, D, and Shaw, J. *Medicine and Science in Sports and Exercise* 1995; 27: S68.

> Significant loss of bone density in the femoral neck and lumbar spine was detected over an eight months period in elite female distance runners. This decrease is related to intensity and volume of endurance activity and occurred in amenorrheic as well as eumenorrheic runners. The authors theorize that the bone remodeling cycle is altered in favor of resorption due to insufficient recovery time. The women in this study had a calcium intake that averaged 700 mg/day, considerably below the RDA recommended intake.

Low Bone Density at Axial and Appendicular Sites in Amenorrheic Athletes. Myburgh KH, Bachrach LK, Lewis B, Kent K, and Marcus R. *Medicine and Science in Sports and Exercise* 1993; 25(11) :1197-1202.

> Researchers studied 12 amenorrheic and 9 eumenorrheic (normally menstruating) women athletes and found that bone density was lower in amenorrheic subjects at several sites. The conclusion was that low bone density in athletes with amenorrhea is not limited to the spine, but is also present in weight-bearing bones such as the hip, legs, and total body.

Running Induces Menstrual Disturbances But Bone Mass is Unaffected, Except in Amenorrheic Women. Hetland ML, Haarbo J, Christiansen C, Larsen T. *Journal of the American Medical Association* 1993 July; 95(1) :53-60.

> Two hundred and five female runners were investigated as to the prevalence of exercise-related menstrual and sex hormonal disturbances and the effect of exercise on bone mass and metabolism. The prevalence of amenorrhea increased from 1% in the normally active subjects to 11% in the elite runners. In the large majority of the runners, no skeletal affection was found despite significant sex hormonal and menstrual disturbances. Only the runners with amenorrhea might be at increased risk of osteoporosis.

Bone Gain in Young Adult Women. Recker RR, Davies KM, Hinders SM, Heany RP, Stegman MR, Kimmel DB. *Journal of the American Medical Association* 1992 November 4; 268(17) :2403-8.

This study looked at bone mass gains over 5 years in 156 healthy, non-pregnant, white female college students. The conclusion was that bone mass gain is positively influenced by modest increases in calcium intake adjusted for protein intake, in self-selected physical activities and in the use of oral contraceptives in the third decade of life.

Factors Associated with Stress Fractures in Young Army Women: Indications for Further Research. Freidi KE, Nuovo J. *Military Medicine* 1992 July; 157(7) :334-338.

The authors surveyed 2,312 active duty Army women for the prevalence of ever having been diagnosed with a stress fracture (16.1% of respondents) and examined the relationship between surveyable risk factors for low bone density and this self reported stress fracture history. Current smoking, previous history of amenorrhea, and known family history of osteoporosis were significantly associated with self-reported stress fractures.

Menstrual History as a Determinant of Current Bone Density in Young Adults. Drinkwater BL, Bruemner B, Chestnut CH 3d. *Journal of the American Medical Association* 1990 January 26; 263(4) :545-8.

Four years of research on 97 women ages 18-38 showed that young amenorrheic athletes have significantly lower vertebral bone density than control subjects with normal menses. A significant relationship was found between current vertebral density of these women and their past and present menstrual patterns. A combination of menstrual patterns and body weight predicted 43% of the total variation in lumbar density. This bone loss was reversed when amenorrheic women decreased their activity levels or gained a small amount of weight.

Menstrual Function and Bone Mass in Elite Women Distance Runners. Marcus R, Cann C, Madvig P, Minkoff J, et al. *Annals of Internal Medicine* 1985; 102(2) :158-163.

Bone mass and metabolic features were studied in 17 women distance runners. Bone density of the spine was lower in amenorrheic runners than in those with normal menstrual periods, but higher than in those with amenorrhea who are not physically active. Running-related fractures were more frequent in amenorrheic women. The conclusion was that intense exercise may reduce the impact of amenorrhea on bone mass; however, amenorrheic runners remain at high risk for exercise-related fractures.

Exercise-Induced Amenorrhea and Bone Density. Lindberg JS, Fears WB, Hunt MM, Powell MR, Boll D, Wade CE. *Annals of Internal Medicine*. November 1984; 101(5) :647-648.

Investigators examined the effects of exercise-induced amenorrhea on bone density in female runners. Bone loss occurred in women with exercise-induced amenorrhea.

STRESS FRACTURES IN MILITARY TRAINING

Quantitative ultrasound predicts stress fracture risk in female army recruits. Kimmel BD, Lappe JM, Hise L, Lauren MJ, White M, Stegman MR, Raab-Dullen DM. Osteoporosis Research Center, Creighton University; Omaha, NE and Orthopedics Department; Fort Leonard Wood, MO. Unpublished.

> The purpose of this study is to predict the risk of stress fracture during routine Army basic training by using ultrasound bone mass measurement tests in 890 female Army recruits. The stress fracture incidence was 4.6%, 41 of the recruits fracturing after 19 days of training. It was found that a recruit with broadband ultrasound attenuation (BUA) of 63 has a 1-in-8 chance of having a stress fracture during basic training.

Cigarette Smoking, Physical Fitness, and Injuries in Infantry Soldiers. Reynolds KL, Heckel HA, Witt CE, Martin JW, and others. *American Journal of Preventive Medicine* 1994 May; 10(3) :145-50.

> This study evaluated a light infantry unit prospectively and following it throughout one year of infantry training and operations. Fifty-five percent of the soldiers experienced one or more training related injuries. Fractures accounted for the greatest number of days of limited duty. Logistic regression showed that cigarette smoking and low endurance levels were independent risk factors for training injuries. A number of modifiable injury risk factors were identified, suggesting that a number of these injuries may be preventable.

West Point Cadets. Copley JB, Lindberg, JS, Wade, C, Ryan, J. Ochsner Clinic, Department of Internal Medicine,Section of Nephrology. Unpublished.

> Male and female West Point cadets were followed over a your-year period and tested every six months. Bone density was found to dropped during the first year of service. The loss was greatest during the first six months when the cadets partook in the most strenuous exercise. The authors hypothesize that exercise-induced injury is associated with decreased bone density.

Intrinsic Risk Factors for Exercise Related Injuries Among Male and Female Army Trainees. Jones BH, Bovee MW, Harris JM 3d; Cowan DN. *American Journal of Sports Medicine* 1993 Sept-Oct; 21(5) :705-10.

> To identify intrinsic risk factors 391 army trainees (124 men, 186 women) were studied for eight weeks. Women had significantly higher incidence of time-loss injuries than men. Men with histories of inactivity and with higher body mass index were at greater risk of injury than other men, as were the shortest women.

Stress Fractures in the Lower Extremities of Soldiers in Basic Training. Pester S, Smith PC. *Orthopaedic Review* 1992 March; 21(3) :297-303.

In a four year study, 1,338 stress fractures were confirmed in total training population of 109,296 for an incidence of 0.96%, .91% of the men and 1.09% of the women experienced fractures. Female soldiers suffered more than twice the number of bilateral stress fractures than men. Modifications in the physical training aimed at eliminating continuous, high impact activities during high risk weeks resulted in a 12.73% drop in fracture incidence (decreases of 7.32% in women and 16.19% in men).

EATING DISORDERS AND BONE DENSITY

Mineral Balance and Bone Turnover in Adolescents with Anorexia Nervosa. Abrams SA, Silber TJ, Estaban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yergey AL. *Journal of Pediatrics* 1993 August;123(2) :326-31.

Seven female adolescents with anorexia nervosa were evaluated to determine whether calcium metabolism was affected by their disorder. The percentage of absorption was lower in subjects with anorexia nervosa than in the control group. Calcium kinetic studies demonstrated a decreased rate of bone formation and an increased rate of bone resorption. The authors hypothesize that improvement in bone mineralization during recovery from anorexia nervosa will require resolution of hormonal abnormalities.

Predictors of Osteopenia in Premenopausal Women. Hay PJ, Delahunt JW, Hall A, Mitchell AW, Harper G, Salmond C. *Calcified Tissue International* 1992;50 :498-501.

Sixty-nine female anorexia patients age 20-40 and thirty-one controls were given spinal bone density tests. Bone density was significantly lower in the patient group. Bone density correlated significantly with duration of illness, amenorrhea, and weight histories, but not with calcium intake or exercise levels. The most important predictor was duration of low calcium intake during adolescence. Regular exercise and adequate dietary calcium did not appear to prevent bone loss related to prolonged periods of low weight and amenorrhea.

Recovery From Osteopenia in Adolescent Girls with Anorexia Nervosa. Bachrach LK, Guido D, Katzman D, Marcus R. *Journal of Clinical Endocrinology and Metabolism* 1991; 72(3) :606.

Decrease in bone mass is a complication of anorexia. The bone mass was measured in 15 anorexia patients at the start and again at 12-16 months. Despite gains in bone density for some, 8 patients had low bone mass in the spine and/or whole body. Changes in body mass, weight, and height were significant predictors of changes in bone density. Low bone mass persisted following recovery, indicating that bone mass deficits acquired in adolescence may not be completely reversible.

Mechanics of Osteoporosis in Adult and Adolescent Women with Anorexia Nervosa. Biller BM, Saxe V, Herzog DB, Rosenthal DI, Holzman S, Klibanski A. *Journal of Clinical Endocrinology and Metabolism* 1989; 68(3) :548-54.

Twenty-six women and seven adolescents were studied to determine the consequences of developing anorexia nervosa before attaining peak bone mass. Adult patients had significantly reduced spinal bone mass. Those patients who experienced amenorrhea before age 18 had significantly lower spinal bone density than those developing amenorrhea later. The study concluded that both the onset of anorexia nervosa before the attainment of peak bone mass and prolonged duration of amenorrhea result in the most significant loss of bone mass.

SMOKING AND OSTEOPOROSIS

Cigarettes Found to Boost Women's Osteoporosis Risk. Waldholz M. *Wall Street Journal* February 10, 1994.

Cigarette smoking significantly increases a woman's risk of developing the bone-thinning disease osteoporosis in this report on research conducted by Ego Seeman and John Llewelyn at the University of Melbourne. The researchers studied 41 pairs of twins, one who smoked and the other who did not. They found the smokers had 1-2% bone loss for every ten years smoking while the non-smoking twin did not. The more frequent smokers had bone losses up to 5-10% enough to sharply raise the risk of fracture.

Long-Term Bone Loss in Men: Effects of Genetic and Environmental Factors. Slemenda CW, Christian JC, Reed T, Reister TK, Williams CJ, Johnston CC. *Annals of Internal Medicine.* 1992; 117 :286-291

This was a 16 year cohort study of 111 male veterans each of whom was a twin. Bone mass and environmental factors including cigarette smoking, alcohol consumption, physical activity, dietary calcium intake, and use of thiazide diuretics was measured at baseline and 16 years later. Two environmental factors emerged as consistant independent predictors of bone loss. Those who smoked at all lost more bone over 16 years than did the non-smokers. Similar associations were observed between alcohol and bone loss. The adverse effects of cigarette smoking and alcohol consumption beyond minimal levels have been established for many chronic diseases and now must include osteoporosis in both men and women.

IMPACT OF CALCIUM DIETARY INTAKE ON BONE MASS

Calcium Supplementation and Bone Mineral Density in Adolescent Girls. Lloyd, T. et al, Journal of American Medical Association 1993 August 18; 270(7):841-844.

A double-blind, placebo-controlled trial of the effect of 18 months of calcium supplementation on bone density and bone mass in 94 girls resulted in a significant increase in total body and spinal density. The increased intake was from 80% of the recommended daily allowance to 110%.

Dietary Calcium and Bone Density Among Middle-Aged and Elderly Women in China. Hu, JF, et al., American Journal of Clinical Nutrition 1993; 58:219-27.

> Association between dietary calcium and bone status were investigated in 843 Chinese women from five rural counties where dietary calcium varied considerably. Analysis for all counties combined showed that bone mass were correlated positively with total calcium. The results strongly indicated that dietary calcium, especially from dairy sources, increases bone mass in adult women by facilitating optimal peak bone mass earlier in life.

DEPARTMENT OF THE ARMY
U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
FORT DETRICK, FREDERICK, MD 21702-5012

November 19, 1995

REPLY TO ATTENTION OF
Army Operational Medicine
Research Program

Ms. Sandra C. Raymond
National Osteoporosis Foundation
1150 17th Street NW, Suite 500
Washington DC 20036-4603

Dear Ms. Raymond,

Thank you for your interest in the Army Operational Medicine Research Program. I understand that my predecessor, Colonel Gifford, had spoken to representatives of the Osteoporosis and Paget's Foundations about the possible competitition of research funds in this area. However, the funds for osteoporosis research were not released to us.

As you may know, bone health is a key military readiness issue which is being addressed in our research program. This is particularly an issue for young servicewomen who are still accruing bone mineral. Clearly, the way we feed and train our young women may influence their risk for osteoporosis later in life. Of immediate concern to the military is the similarity between factors which predispose a woman to osteoporosis risk and the risk of stress fracture in basic training, including factors such as cigarette smoking, low body weight, and amenorrhea. Studies of women in Army basic training, Marine recruit training, and plebes at West Point all indicate rates of stress fracture which are 10-15% of the women, compared to 1-3% of men in the same study.

In the Defense Womens Health Research Program (DWHRP94), we targeted stress fractures for concerted research likely to have an impact on military readiness. Three extramural projects were funded, for a total of $1.8 M (enclosure). The U.S. Army Research Institute of Environmental Medicine has also conducted research in this area, but there is much more to be done, including intervention studies involving training, diet, and hormones, and bisphophonates.

I welcome your support of this important research. We will keep you informed of the results of our research. My point of contact for further discussion is Major Karl Friedl, (301) 619-7301.

Sincerely,

Frederick W. Hegge

Frederick W. Hegge, Ph.D.
Director, Army Operational
Medicine Research Program

fax 703 697 4197

HOGAN & HARTSON
L.L.P.

CHRISTINE M. WARNKE, PH.D.
GOVERNMENTAL AFFAIRS ADVISOR
DIRECT DIAL (202) 637-5645

MEMORANDUM

COLUMBIA SQUARE
555 THIRTEENTH STREET, NW
WASHINGTON, DC 20004-1109
TEL (202) 637-5600
FAX (202) 637-5910

January 5, 1996

PRIVILEGED AND ~~CONFIDENTIAL~~

TO: Debbie Fein, The White House

FROM: Christine Warnke

RE: Meeting on January 17, 1996 at the White House

This is to follow-up our conversation regarding the Department of Defense Bone Disease Research Funds. Attached is a letter initiated by Senator Bill Cohen and signed by ten other Senators to Defense Secretary William Perry regarding the DOD funding which I believe is self-explanatory. Some issues we want to address at our meeting of January 17, 1996, include the following questions:

What kind of peer review system will the Department of Defense devise for these research projects?

What are DOD's programmatic goals?

I will call you next week so we can further discuss this meeting in more detail. Also enclosed is a detailed fact sheet on Osteoporosis and Defense and an article entitled "Factors Associated With Stress Fractures in Young Army Women: Indications for Further Research."

DETERMINED TO BE AN
ADMINISTRATIVE MARKING
INITIALS: MA DATE: 2/25/14

United States Senate
SPECIAL COMMITTEE ON AGING
WASHINGTON, DC 20510-6400

December 8, 1995

The Honorable William Perry
Secretary of Defense
Department of Defense
The Pentagon
Washington, D.C. 20301

Dear Secretary Perry:

We are writing to express our support for the Department of Defense to initiate its research efforts on osteoporosis and bone related diseases funded by Congress in 1995. In the Fiscal Year 1995 Defense Appropriations legislation, funds totaling $5 million were appropriated for the Department of Defense to carry out osteoporosis and bone related disease research. Unfortunately, DOD continues to delay the release of these much needed funds.

Osteoporosis is a major health threat for 25 million Americans, 80 percent of whom are women. In the United States today, seven to eight million individuals already have the disease and 17 million more have low bone mass, placing them at increased risk for osteoporosis. Further, a great deal more research needs to be done in order to determine the causes of stress fractures in both servicemen and women.

We believe the need to expand present medical research on osteoporosis and bone related diseases is evident. Findings that emanate from such DOD efforts will not only assist our active duty forces but will also serve to find the means to treat the millions of Americans who are at high risk or have developed this debilitating disease. We ask that the funds already allocated by Congress be released so our military personnel can benefit from this much needed research.

In light of the 197,291 servicewomen in the Armed Forces and the trend toward more women entering the military, we strongly believe these diseases pose significant defense health risks and warrant the release of these important funds.

Thank you for your attention to this matter and please keep us informed of your efforts in this area.

Sincerely,

William S. Cohen

Daniel K. Akaka

Olympia J. Snowe

Jesse Helms

Dale Bumpers

Daniel K. Inouye

Thomas A. Daschle

Carol Moseley-Braun

Bill Frist

Tom Harkin

Bill Bradley

OSTEOPOROSIS AND DEFENSE

Osteoporosis affects 25 million Americans, 80 percent of whom are women. Each year there are 1.5 million osteoporotic bone fractures including more than 280,000 hip fractures, 500,000 vertebral fractures, 250,000 wrist fractures and the balance at other bone sites. The medical costs associated with this disease exceed $10 billion and are expected to dramatically increase as the population ages. Without intervention, the costs in the Year 2010 will exceed $60 billion and are expected to reach $240 billion by the Year 2050. Recently, the University of Southern California's Gerontology Center reported that the costs associated with osteoporosis and Alzheimer's disease threaten to swamp the medicare system.

Recently, we contacted the VA data center and found that, in 1993, there were more than 2,600 men over the age of 65 admitted to the VA hospital system due to hip fractures attributable to osteoporosis. These admissions accounted for 66,000 hospital care days. We have now requested information on the number of women who have received VA medical care for osteoporosis-related hip fractures. The average acute care cost of one hip fracture alone is $40,000. Since women are four times more likely to develop hip fractures, it is likely that the total number of admissions is much greater than the number cited above. It is unknown how many more men and women have received medical care for osteoporosis-related fractures of the spine, wrist and/or other bones.

Osteoporosis is essentially preventable and treatable; but, the disease must be prevented in 20 and 30 year olds. For once bone is lost, it cannot be replaced. Bone loss is progressive and irreversible: prevention is the key!

Presently, there are 197,291 servicewomen in the Armed Forces. This number represents 12.1 percent of the total active duty forces. As more women enter the armed services, osteoporosis will increasingly become a defense health issue. For many women, excessive physical training causes amenorrhea and leads to the loss of the protective effect of estrogen on bones. This bone loss eventually causes osteoporotic fractures. There is also evidence that males suffer activity-related hypogonadism, which may also lead to osteoporosis and fractures.

To address the problem, basic and clinical medical research is needed to:

- Overall, strengthen basic and clinical research programs to uncover the pathogenesis of osteoporosis, increase understanding of the basic cellular mechanisms by which bone remodeling is controlled
- Conduct studies on the pathogenesis and treatment of glucocorticoid-induced osteoporosis
- Study activity-related bone loss in women and men related to high-level physical activity
- Determine levels of activity which improve the skeleton, not impair bone metabolic function
- Study the parameters of short-term morbidity associated with musculoskeletal injuries related to training
- Study medical interventions which may offset bone loss in men and women
- Determine the etiology of hypogonadism in male recruits
- Determine which bone sites are most affected by physical training issues (excessive training usually causes low spinal bone mass, what happens at the hip?)
- Examine the level of musculoskeletal stress fractures due to equipment worn (boots) or carried during training

MILITARY MEDICINE, 157, 7:334, 1992

Factors Associated with Stress Fracture in Young Army Women: Indications for Further Research

*MAJ Karl E. Friedl, MSC USA**
Jennifer A. Nuovo, MD†
Troy H. Patience, DAC†
LTC Joseph R. Dettori, AMSC†

Several factors which affect bone density and predict risk of osteoporosis (e.g., ethnic origin, amenorrhea) are reportedly associated with a higher incidence of stress fracture in active premenopausal women. The authors surveyed 2,312 active duty Army women for the prevalence of ever having been diagnosed ("told by a doctor") with a stress fracture (16.1% of respondents) and examined the relationship between surveyable risk factors for low bone density and this self-reported stress fracture history (self-reported SF). Current smoking, previous history of amenorrhea (menses absent > 6 months), and known family history of osteoporosis were significantly associated with self-reported SF, while black ethnic origin was a protective factor. These data suggest hypotheses of stress fracture pathogenesis in Army women which bear further testing.

Introduction

Women in the United States now participate in exercise programs more than ever before. A subset of these women will develop stress fractures as a consequence of the increase in weight-bearing exercise.[1] Women are at substantially higher risk for stress fracture than men. This difference has been noted in military basic training, where 10–12% of women suffer stress fractures, compared to an incidence of 1–3% of men participating in the same training.[2-4] Bone remodeling is part of a normal response to physical stressors and this is generally expected to result in a stronger bone;[5,6] however, in some susceptible individuals, a debilitating fracture occurs in remodeled sites before the changes are complete.[4,7] Recent research attention has been focused on stress fracture in amenorrheic athletes, where menstrual status appears to play a role in determining which women will be most susceptible to stress fracture.[8] Presumably this risk is greater in individuals with lower bone densities and may also be related to other factors which predict risk of osteoporosis in women. These factors include Asian or white race,[9,10] family history of osteoporosis,[11] underweight,[12,13] exercise,[14] and factors related to a reduced estrogen level such as smoking,[15] episodes of amenorrhea,[16] and post-menopausal status.[17]

We conducted a pilot study to investigate the association of surveyable factors which have been linked to reduced bone density to self-reported history of medically diagnosed stress fracture (self-reported SF). This was performed with an Army population consisting primarily of premenopausal physically active women lacking significant illness.

Methods

A questionnaire was developed which asked 18 questions about the presence of factors associated with reduced bone density. The questions were brief and called for simple answers. An initial version of the questionnaire was administered to 50 soldiers who were then interviewed by a physical therapist (JRD) about their responses; the final form was a refinement based on this test survey.

We defined self-reported SF history as a positive response to the question: "Has a doctor ever told you that you had a stress fracture?" A few of these responses were reclassified as negative when the subsequent question ("If yes, what part of your body?") turned up improbable diagnoses more related to psychological stress, such as "brain" and "stomach." The types of stress fracture most likely to be detected and correctly diagnosed at a general medical treatment facility would generally be categorized as symptomatic, either with debilitating pain or frank fractures. Since medical records were not available in this anonymous survey, these self-reported SF cases could not be confirmed. In addition to misinterpretation of the diagnosis by some respondents, an unknown number of disorders may have been misclassified as stress fracture, including periostitis, compartment syndromes, infections, pre-existing bone problems (bone cysts, old injuries), or muscle fatigue problems.

---

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The views, opinions, and findings in this report are those of the authors and should not be construed as an official Department of Army position, policy, or decision.

This manuscript was received for review in January 1991. The revised manuscript was accepted for publication in August 1991.

Thus, in this study we refer to these putative stress fracture diagnoses as self-reported SF with the understanding that these are unconfirmed diagnoses.

We defined amenorrhea as a 6-month absence of menses not associated with pregnancy. Family history of osteoporosis was indicated from "did your mother or your grandmother develop a hunched-over appearance or break their hips?", if this information was known. Weight trends were assessed by asking the women if they had ever exceeded Army weight standards [i.e., body mass index > 23–24 kg/m²] or if they had ever been told that they were underweight. Exercise habits were investigated by "how many days per week do you exercise?" and, since running is the primary form of organized exercise in the Army, we also asked "how many miles per week do you run?" The presence or absence of other factors were determined with simple "yes" or "no" questions.

The questionnaire was mailed to the duty addresses of every active duty female soldier at Fort Lewis, Washington in July 1987 (N = 2,462). The questionnaire was accompanied by a short letter signed by a female Army physician (JAN) soliciting participation in a study "important to the health of female soldiers." Soldiers were also asked to return separately an identifying postcard indicating whether or not they planned to return a survey form. Completed surveys were returned by 1,295 soldiers: 1,288 postcards were also returned, including 8 which indicated that the subjects would not participate. Four weeks after the first mailout, a second copy of the survey was sent to 1,092 soldiers who were presumed to have been reached by the first survey but had not returned a postcard. They were encouraged to return a survey if they had not already done so. A total of 1,630 out of 2,312 (70.5%) deliverable questionnaires were returned within 10 weeks of the first mailout and these were used in the analysis.

Factors associated with reported stress fractures were contrasted using a contingency table format with a chi-square test. Logistic regression was performed to determine the strength of the association between significant factors and stress fractures. The Mantel-Haenszel chi-square test was used to examine the effect of age and ethnic origin on the other factors (BMDP87, Los Angeles, California).

Results

The mean age in the survey sample was 26.1 ± 5.8 (SD) years (median age: 24 years; range: 18–52). The ethnic breakdown of respondents was 57.1% non-Hispanic white, 32.8% black, 5.0% Hispanic, 2.2% Asian, and 2.9% other or unspecified. In this sample, 16.1% of women had self-reported SF histories. The most prevalent location for the injury was the leg (53.2% of stress fractures reported) (Table I). Other known characteristics of the survey sample are presented in Table II.

Table II compares the percentages of women with self-reported SF in subpopulations of women with or without factors which affect bone density (chi-square test). Analysis by stepwise logistic regression yielded five factors independently associated with self-reported SF: history of amenorrhea, current cigarette smoking, non-black ethnic origin, known family history of osteoporosis, and young age. Age was included in the logistic analysis as a continuous variable and the skewed distribution was normalized with a log transformation. All of

TABLE I

LOCATION OF MEDICALLY DIAGNOSED STRESS FRACTURES

Location	Number	Proportion of all Stress Fractures (266)	Prevalence in Overall Sample (1,630)
Pelvis	15	5.6%	< 1.0%
Hip/thigh	23	8.7	1.4
Leg	140	53.2	8.6
Foot	74	28.1	4.5
Other	11	4.2	< 1.0
Total	263	99.9%*	16.1%

*Total is less than 100% due to rounding.

these terms and the likelihood ratio for the logistic model were significant at a probability level of 0.005 or less.

Based on the logistic analysis, the probability of self-reported SF ranged from 31.6% in a non-black smoker with episodes of amenorrhea and a family history of osteoporosis, down to 8.0% for a black non-smoker with normal menstrual history and a negative family history—a 4-fold difference. Relative risks (and 95% confidence interval) determined from the logistic analysis for amenorrhea, smoking, non-black ethnic origin, and family history were 1.36 (1.25–1.48), 1.32 (1.23–1.41), 1.28 (1.17–1.39), and 1.25 (1.16–1.35), respectively.

Age was a significant covariable for the prevalence of self-reported SF. Thus, from the logistic regression, older women with none of the four other risk factors would have a predicted prevalence as low as 1.5%. The actual prevalence in our sample for all women over age 40 (N = 42) was 1.4%, compared to the highest overall prevalences of 19.6% for women aged 22–23 (Fig. 1). This is a likely consequence of selective processes in this specific military population, as will be discussed. Dividing the sample roughly in half, at age 25, each of the other four factors was shown to be significantly affected by age (Mantel-Haenszel, $p < 0.001$). Odds ratios from the individual factor chi-square tables were similar to but slightly higher than those derived from the logistic analysis (Table III). Amenorrhea had a significant effect on stress fracture prevalence only in the younger women (29.9 vs. 16.0%, $p < 0.001$) compared to women > 25 years old (18.2 vs. 12.7%, $p = 0.12$). Age was also a significant cofactor for underweight, with only the younger women demonstrating a significant relationship between self-reported SF and being underweight ($p < 0.05$; Mantel-Haenszel test, $p < 0.05$). Other factors such as parity and use of oral contraceptives were age-related (Fig. 2) but had no association with prevalence of self-reported SF.

Black women were significantly more likely to have had children (51.5 vs. 36.8%; $p < 0.001$), were more likely to use oral contraceptives (40.9 vs. 31.6%; $p < 0.001$), and were less likely to be current smokers (32.1 vs. 37.8%; $p < 0.001$), all factors which have been reported to be protective against stress fracture or osteoporosis. Only 12.0% of black women reported a family history of osteoporosis, compared to 38.2% of non-black women. Nevertheless, a positive family history of osteoporosis was associated with a 10% higher prevalence of self-reported SF, with no difference between blacks and non-blacks (p = 0.62). Ethnic differences in stress fracture were apparent only when family history of osteoporosis was negative ($p < 0.01$; Mantel-Haenszel chi-square test, $p < 0.01$).

TABLE II

PREVALENCE OF STRESS FRACTURE IN ASSOCIATION WITH SURVEYED FACTORS RANKED IN ORDER OF FACTOR PREVALENCE IN THE SAMPLE

Factor	% of Total with Factor	% with History of Stress Fracture: Factor Present	% with History of Stress Fracture: Factor Absent	
Ethnic origin (white or Asian)	87.3	18.5	11.3	***
Nulliparity	58.4	16.1	16.2	
Gynecological age ≤ 20 (1)	(16.6)	19.3	14.5	
More than 2 births (1)	(12.7)	15.4	17.0	
Age (≤ 25 years)	44.8	18.2	13.6	**
Cigarette smoking (ever)	55.1	19.4	12.0	***
Cigarette smoking (current)	34.6	21.9	13.1	***
Have smoked for > 10 years (2)	(30.4)	24.8	20.4	
More than one pack/day (2)	(19.2)	24.6	20.7	
Current oral contraceptive pill use	34.6	17.6	15.1	
Ever on the Army Weight Control Program (BMI > 23–24 kg/m²)	31.0	16.9	15.7	
Family history of osteoporosis	29.8	21.8	13.5	***
Running exercise (> 10 miles/week)	21.0	19.0	15.4	
Ever told that they were underweight	16.9	20.5	15.4	*
History of amenorrhea (episodes of ≥ 6 months)	14.9	22.7	13.4	***
Late menarche (> 16 years old)	3.6	19.0	18.1	

Notes: chi-square test: significance: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
Subsamples: (1) parous women (n = 698); (2) current smokers (n = 581).

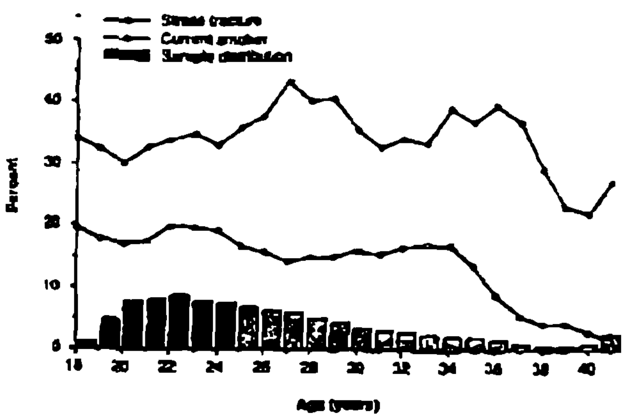

Fig. 1. Distribution of respondents by age (bars) and the prevalence of self-reported SF and current smoking. The line graph data are expressed as a three-point running mean.

Fig. 2. Prevalence of parity, oral contraceptive use, and menstrual irregularity by age in active duty Army women. Data are expressed as a three-point running mean.

TABLE III

ODDS RATIOS OF FACTORS ASSOCIATED WITH STRESS FRACTURE STRATIFIED BY AGE

Factor	Age Group	Odds Ratio	Probability	Pooled Odds Ratio (95% Confidence Interval)
Amenorrhea history	≤25	2.24	0.0002	1.93 (1.37–2.72)
	>25	1.53	0.12	
Current smoker	≤25	1.96	0.0001	1.91 (1.45–2.51)
	>25	1.84	0.005	
Ethnic origin (white/Asian)	≤25	1.78	0.003	1.82 (1.33–2.50)
	>25	1.94	0.02	
Family history	≤25	1.66	0.01	1.88 (1.38–2.55)
	>25	2.22	0.0007	

A positive history of amenorrhea eliminated the relation between smoking and stress fracture, with more stress fractures in smoking vs. non-smoking women without history of amenorrhea (20.3 vs. 11.6%, $p < 0.001$) but with no differences between smoking and non-smoking women with a history of amenorrhea (28.6 vs. 21.8%, $p = 0.23$) (Mantel-Haenszel test, $p < 0.001$). Smoking had a comparable effect on the relation between amenorrhea and self-reported SF, with a significant relation in non-smokers ($p < 0.001$) but not in smokers ($p = 0.08$) (Mantel-Haenszel test, $p < 0.001$). More women had experienced episodes of amenorrhea in the subpopulations of women who had (ever) been told that they were underweight (23.7 vs. 13.2%) and who were runners (> 10 miles/week) (20.3 vs. 13.4%, $p < 0.05$).

Discussion

The prevalence of self-reported SF in the women in this survey (16.1%) is consistent with other reports. Eleven percent of the women surveyed had both a history of stress fracture and reported that during basic training they had bone pain which was sufficiently debilitating that they had to stop running. Although we did not specifically ask if stress fracture was diagnosed in basic training, it is probable that many of the self-reported SFs occurred in basic training, at a rate which is comparable to the 10.5% observed in a group of 114 female Marine recruits during basic training,[18] 10.0% observed in the first 8-week training period at the U.S. Military Academy,[3] and 11.3% observed in 186 Army recruits in basic training.[4] Assuming in the worst case that all of our nonrespondents were disinterested women with no history of stress fracture, we would still have a self-reported SF prevalence of greater than 10%.

Most previous studies of stress fracture have been conducted with elite athletes and little is known about risks to the general population. Although our sample is skewed toward younger women and it excludes individuals with conditions which significantly affect physical performance since this is a condition of continued Army employment, this study yields information about healthy young women who are otherwise typical of the general U.S. population. Generalization about older active women must be made with caution because of the selective processes which determine their presence in this sample, and because the intensity of physical training for women during Army basic training (where stress fractures tend to emerge) increased markedly in 1978.

The association of smoking with self-reported SF is one of the most interesting findings to emerge from this study. Cigarette smoking has been associated with reduced bone mineral content and osteoporosis,[15,19] although some studies have failed to demonstrate a connection.[20] Our results provide the first suggestion of such a relationship to stress fractures in a population which is almost entirely premenopausal. Smoking reduces serum estrogen levels in a dose-related relationship, possibly through a nicotine-induced increase in hepatic metabolism,[21,22] and this reduction in estrogen levels has been linked with a trend to reduced bone mineral density in smokers.[23] It may also be important that our smokers had a higher prevalence of self-reported SF than women who were former smokers since this suggests that smoking may be a modifiable risk factor. We did not find any additional differences in self-reported SF between duration of smoking (analyzed as a continuous variable; data not shown) or smoking more than one pack per day in the current smokers.

Amenorrhea is also a factor identified in this study which may be modifiable through physician intervention. Our data confirm previous findings in collegiate women athletes, where stress fractures were observed in 24% of women with irregular or absent menses but in only 9% of the women with normal menses.[6] Like smoking, the effect on bone is presumably produced by episodes of hypoestrogenism.[16,11,24] Indeed, women with a history of amenorrhea did not have a significantly higher prevalence of self-reported SF if they also smoked, nor was there a significant association between amenorrhea and self-reported SF in women who smoke, suggesting a single mechanism by which these two factors may produce a marked susceptibility to self-reported SF. This effect on bone density appears to be reversible with a resumption of menses.[25] The data suggest that amenorrhea is a symptom which may signal higher risk of bone injuries in women engaged in vigorous weight-bearing activities, such as running or marching, and measures should be taken to return such individuals to normal menstrual patterns. Protective measures might include reduced training volume or the prescription of estrogens (with opposing progestagens) by a physician if a significant reduction in bone density is established.

Lloyd et al.[6] found that risk of stress fracture was lower in those who used oral contraceptives. We did not find any significant relation to the use of oral contraceptives, but this may be related to the difference in prevalence of amenorrhea in our study population. The prevalence of amenorrhea may be high in some athletes and, in these women, the low-dose estrogen of many contraceptive preparations may offer some protection against bone loss. In contrast to athlete samples, only 14.9% of our population reported amenorrhea "ever" and only 1.3% of the non-pregnant women in our sample were currently amenorrheic (>6 months since last menses at the time of survey); 10% of our respondents were currently pregnant. This rate of amenorrhea is similar to the point prevalence rate of 1.8% reported in a Swedish survey of a normal community.[26]

In our study, women running over 10 miles/week or having been told they were underweight were also more likely to have a history of amenorrhea, but these factors appear to be only loosely associated. Exercise serves as the stimulus for bone remodeling but whether this will result in an increase in bone density or in a stress fracture appears to be dependent on other factors, such as history of amenorrhea. This is suggested by our data, and by the results of studies of female athletes where the rates of stress fracture in eumenorrheic exercising women were unremarkable.[8] Intense exercise may be involved in amenorrhea, as evidenced by the return of menses in some amenorrheic women who reduce their exercise,[27] but amenorrhea is not a necessary consequence of intense exercise.[28] Similarly, low weight (or low body fat) does not necessarily produce amenorrhea.[29] These three factors may be non-causally associated as common aspects of a behavioral and/or hypothalamic disorder.[30] Underweight was associated with an increased likelihood of self-reported SF in the younger women (<25 years old) but, although body weight is a factor in bone mass,[31,32] underweight did not emerge as an independent factor associated with self-reported SF in this study.

Positive family history is recognized as a risk factor in osteoporosis,[11] and a reduced bone mass has been demonstrated in relatives of osteoporotic patients.[33] Family history was a factor associated with an increased prevalence of self-reported SF in both black and non-black women in our study. Ethnic origin was a second unrelated hereditary factor associated with self-reported SF. The reduced risk of osteoporosis in black women is associated with a greater bone density, perhaps as a result of reduced osteoclast activity.[34] Whether or not this reduced excavation of bone persists during an exercise-induced remodeling remains to be demonstrated, but the achievement of a higher bone mineral density in black women is of itself likely to be protective of stress fracture, an association confirmed in this study. Brudvig et al.[35] found that the 1-year incidence of stress fracture was 1.4 in black women compared to 11.8 in white women in a young population of basic recruits reporting to a physical therapy clinic. While the incidence was lower in males, there was still a lower incidence in black males than white males. Our data confirm this protective effect of black ethnicity on stress fracture.

This study suggests hypotheses for further investigation, specifically the possibility that smoking, amenorrhea, and family history of osteoporosis are risk factors for stress fracture in young women, while black ethnic origin may be a protective factor.

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