Identifying Fracture Risk in Postmenopausal Women

To the Editor: Dr Siris and colleagues[1] found that many asymptomatic postmenopausal women have previously undetected low bone mineral density (BMD). They also confirmed that peripheral bone densitometry, categorized according to T scores, is predictive of subsequent fracture risk in this population.

In this study, and often in clinical practice, the diagnostic threshold of a T score of –2.5 (BMD of 2.5 SDs below the peak adult value) is used. However, Siris et al found that the proportion of women with BMDs below this value varies dramatically by device, from 3.4% with heel ultrasound to 13.5% with finger dual-energy x-ray absorptiometry (DXA). When adjusted for age, weight, and other confounding factors, there was more than a 6-fold difference in the proportion below the threshold. Other studies have shown similar variations in the apparent prevalence of osteoporosis, as well as risk of fractures, when different devices are used with T-score thresholds.[2,3]

The lack of comparability across peripheral devices represents an important barrier to the use of peripheral densitometry in clinical practice and is one reason that central (ie, hip and spine) DXA is recommended by the National Osteoporosis Foundation and the International Society for Clinical Densitometry as the definitive diagnostic tools.[3] Furthermore, the central DXA has been shown to be more precise and predictive of hip fracture than peripheral densitometry or ultrasonography.[4]

While peripheral densitometry may be useful as a general risk assessment tool for patients and their physicians, central DXA of the hip and spine should be performed as the definitive diagnostic tool and used in treatment decision making. Diagnostic categories derived from T scores on peripheral devices are misleading and should not be relied on for treatment decisions.

Dennis Black, PhD
Department of Epidemiology and Biostatistics
University of California
San Francisco

Rachel B. Wagman, MD
Department of Endocrinology, Gerontology, and Metabolism
Stanford University Medical Center
Palo Alto, Calif

1. Siris ES, Miller PD, Barrett-Connor E, et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment. *JAMA.* 2001;286:2815-2822.
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To the Editor: Dr Siris and colleagues[1] found an unexpectedly high prevalence of previously undetected low BMD among postmenopausal women. Their study also confirmed the association of well-accepted risk factors including tobacco, glucocorticoids, and family history of osteoporosis, with low BMD.

Although low body weight is mentioned as an associated risk factor, the authors did not discuss anorexia nervosa. Indeed, the association of anorexia nervosa and osteoporosis is important because more than 50% of young patients with anorexia have osteoporosis,[2] as well as other medical complications.[3] While many of these medical complications are reversed by timely restoration of body weight, osteoporosis may persist even after weight restoration.[4]

Similar to the findings of Siris et al, who found an increased risk of incident fracture within 1 year, the risk of fracture in patients with anorexia nervosa is increased 3-fold vs age-matched controls.[5] This is concerning because anorexia nervosa generally has its onset in adolescence, the same time that peak bone mass should be acquired. Many of these patients will therefore never attain their peak bone mass.

The study of Siris et al should rightfully raise the awareness of primary care clinicians to implement strategies to better identify and treat osteoporosis in postmenopausal women. The same heightened vigilance is especially important for the population of patients with anorexia nervosa. A transient episode of anorexia in youth may permanently impair skeletal integrity, and in contrast to postmenopausal women, exogenous estrogen may not be sufficient to restore bone mass in patients with a history of anorexia nervosa.[6]

Philip S. Mehler, MD
Denver Health Medical Center
Denver, Colo

1. Siris ES, Miller PD, Barrett-Connor E, et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment. *JAMA.* 2001;286:2815-2822.
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Letters Section Editor: Stephen J. Lurie, MD, PhD, Senior Editor.

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In Reply: Drs Black and Wagman note that we reported low BMD at peripheral skeletal sites in terms of T-score thresholds. T scores are the values conventionally reported to physicians who order BMD tests. It was also our belief that reporting the data as T scores would be the most applicable to their clinical experiences with the results presented in terms of these familiar World Health Organization cut points. We concur that for a direct comparison to other studies, expressing fracture risk in terms of relative risk per SD decrease is valuable, and we have previously presented the data in abstract form as relative risk per SD for both the young normal reference ranges for each device and for the mean age of our sample.[1,2]

We also agree that the use of different devices, which incorporate differing technologies, young normal reference ranges, and skeletal sites (varying in cortical and cancellous bone content), contributes to the variation in the absolute numbers of patients with T scores below –2.5. Similar discrepancies in the proportion of women with osteoporosis occur when comparisons are made between spine and hip,[3] the measurements made with central DXA. Although central DXA of the hip is the criterion standard for prediction of hip fracture,[4] access to these larger and more expensive instruments remains a practical problem for many patients. Our data show that all peripheral sites measured had similar ability to predict fracture, as shown by receiver operating characteristic curves.[1,2] The observed areas under the curve for hip fracture, moreover, using forearm peripheral DXA and heel DXA in the National Osteoporosis Risk Assessment are comparable with those reported by Cummings and colleagues for prediction of hip fracture in older women using measurements at the hip.[5] Our data show that a low BMD score obtained on any peripheral device is a warning sign of increased risk for fracture, and that appropriate steps to lower risk are warranted.

We agree with Dr Mehler that anorexia nervosa is an important cause of osteoporosis in young women. In our study we surveyed postmenopausal women, with the intent of identifying those with low body weight. Diverse medical disorders are associated with the risk of osteoporosis and fracture, and a careful medical history and appropriate physical examination are mandatory in evaluating causes of osteoporosis in all patients.

Ethel S. Siris, MD
Columbia University College of Physicians and Surgeons
New York, NY

Financial Disclosure: Dr Siris has received grant support from Merck, Lilly, Aventis; and has been a consultant and on the speaker's bureau for Merck, Lilly, and Alliance for Better Bone Health.

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Breastfeeding vs Formula-Feeding Among HIV-Infected Women in Resource-Poor Areas

To the Editor: In their study of breastfeeding vs formula-feeding among women with human immunodeficiency virus type 1 (HIV-1) in Nairobi, Kenya, Dr Mbori-Ngacha and colleagues[1] found no significant difference in 2-year infant mortality rates. However, I have several concerns about the results of their study, which shows that breastfed infants were more likely to experience the combined end point of death or HIV infection at 2 years.

First, the study's determination of infant HIV-1 status by enzyme-linked immunosorbent assay does not account for the test's capability, which is to look for antibodies rather than the virus itself. Infants in the breastfeeding group might have had high levels due to transmission of the mother's antibodies through breastmilk.

Second, a large number of women in this trial used both breastfeeding and formula feeding. In this study, mixed feeders were assigned to the breastfeeding group, thus creating a substantial bias against success among those in the breastfeeding group.

Third, HIV-1–positive women were selected for participation in this study based on criteria designed to minimize morbidity due to formula use. Despite this selectivity, infants in the formula group did not have better health outcomes.

Fourth, the authors failed to distinguish between the moment of transmission of the virus and the time at which infection progressed to a measurable level. Since there is a time lag between these 2 events, some infections that rise to a measurable level only some months after the infant's birth may in fact have resulted from viruses that had been transmitted prior to or during the birth process.[2] A previous report of data from this trial suggested increasing rates of infection over time even for infants who had not been breastfed.[3]

Nothing in this study showed any good reason for mothers with HIV-1 to choose formula. While we can accept that under ideal conditions, formula might not be as dangerous as it usually is in developing countries, there is as yet no compelling evidence based on observed health outcomes to support the use of formula for infants whose mothers have HIV.

George Kent, PhD
Department of Political Science
University of Hawaii
Honolulu

1. Mbori-Ngacha D, Nduati R, Grace J, et al. Morbidity and mortality in breastfed and formula-fed infants of HIV-1–infected women: a randomized clinical trial. *JAMA*. 2001;286:2413-2420.
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To the Editor: Dr Mbori-Ngacha and colleagues[1] concluded that "formula-fed infants [of HIV-1–positive mothers] had a better outcome than breastfed infants." We disagree with this conclusion because it was based on the assumption that the death rate among breastfed infants will eventually be higher due to their higher likelihood of being HIV-1–positive.

Mbori-Ngacha et al also found a similar incidence of diarrhea in the 2 study groups, which seems to contradict the results of other research.[2,3] However, Table 2 in their article shows that dehydration was more common among the formula-fed infants. It is dehydration, not diarrhea, that leads to mortality in infants.

Although the difference was not statistically significant, more than twice as many HIV-1–positive infants (29% vs 14%) were malnourished in the formula group, and the rate of malnutrition was higher in the formula fed HIV-negative infants as well (11% vs 7%). If this trend were replicated in a larger trial, it could indicate that the negative health effects of formula feeding extend beyond 2 years.

Mbori-Ngacha et al claim that their trial compares breastfeeding with formula feeding. However, it actually compares mixed feeding with mixed feeding because the treatment groups were defined inconsistently and an intent-to-treat analysis was used. Thirty percent of the women in the "formula" group were listed as noncompliant if they breastfed even once, but women in the "breastfeeding" group could use any amount of formula.[4] Consequently, the reported 96% compliance in the breastfeeding group is likely a significant overestimate.

In summary, it is possible that either the apparent higher levels of malnutrition experienced by infants in the formula-fed group or their higher susceptibility to dehydrating diarrhea could result in a higher mortality rate after age 2 years despite the higher prevalence of HIV-1 in the breastfed group.[2,3] Which group will ultimately have a higher mortality rate is at this point merely a matter of speculation. Public policy should not be based on assumptions. Until the true, long-term health consequences of the 2 approaches can be established by more tightly controlled trials with treatment groups that follow up infants with more distinct feeding patterns, we believe that the safest alternative is exclusively breastfeeding.[5]

Andrea Eastman, MA
Marian Tompson
Carol Brussel, BA
Phyll Buchanan
David Crowe, HBSc
Judy LeVan Fram, PT
Jay Hathaway
Valerie W. McClain
Pamela Morrison
Magda Sachs, BA, MA
AnotherLook
Evanston, Ill

Acknowledgment: We thank F. Railhet, MD, for her contributions to this letter.
AnotherLook is a not-for-profit corporation dedicated to gathering information, raising critical questions, and stimulating needed research about breastfeeding in the context of HIV/AIDS.

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To the Editor: In their Editorial that accompanied the study of Dr Mbori-Nagacha and colleagues,[1] Drs Guay and Ruff[2] expressed skepticism about the implementation of formula feeding among HIV-1–positive mothers in resource-poor settings. As a physician in a developing country working on the prevention of perinatal HIV transmission, I would like to express another point of view.

The nutritional, immunologic, and emotional benefits of breastfeeding are essential to the health of children in general. However, there is a significant risk of HIV transmission when an infected mother breastfeeds. Even before the use of antiretroviral drugs, the rate of perinatal transmission of HIV in Europe and North America, in a nonbreastfed population was half the rate of developing countries.[3] In their previous report of this randomized controlled trial, the same authors[4] found in Kenya a significant decrease in mother-to-child transmission of HIV-1 in formula fed compared with breastfed infants, with no additional increased infant mortality attributable to formula feeding. However, their current data[5] revealed increased mortality among HIV-1–infected mothers who breastfed their infants. Given the well designed study by Mbori-Nagacha et al, it is surprising that Guay and Ruff question its conclusions. It is also surprising that an observational study[6] that has shown a higher transmission to have of HIV in mixed-fed vs exclusively breastfed infants seems to have been widely accepted by researchers of the developed world.

I believe that there is a bias (and perhaps a patronizing attitude) on the need to breastfeed in developing countries by researchers from the developed countries. I would like to emphasize that in Brazil, we are achieving low rates of perinatal transmission using antiretroviral drugs in a nonbreastfeeding population without additional mortality.[7] A study in Uganda[8] that investigated the survival rate of a cohort of children infected with HIV has reported extremely high rates (514 deaths/1000 live born infants) of infant mortality at age 2 years, which has no parallel in non-HIV–infected infant populations whether breastfed or not.

The policy of breastfeeding exclusively for 6 months must be viewed with caution because it is not a frequent practice in developing countries. If efforts are being suggested on educating HIV-1 infected mothers in poor countries to practice exclusive breastfeeding for 6 months, why not use the same educational tools to educate them on how to prepare formula safely? Additionally, it has not been proved that an HIV-infected mother's breast milk has immune factors that protect a child.

It is a matter of justice in our globalized civilization that there should be no double standard concerning breastfeeding recommendations with respect to HIV.

Susie Andries Nogueira, MD, PhD
Department of Infectious Diseases
Federal University of Rio de Janeiro
Rio de Janeiro, Brazil

1. Mbori-Ngacha D, Nduati R, Grace J, et al. Morbidity and mortality in breastfed and formula-fed infants of HIV-1–infected women: a randomized clinical trial. *JAMA*. 2001;286:2413-2420.
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In Reply: Dr Kent and Ms Brussel and colleagues question our conclusion that formula feeding resulted in better health outcome among participants in our randomized clinical trial than breastfeeding. We respond by summarizing our key findings.

- Breastmilk transmission of HIV-1 accounted for 44% of all infant infections in a breastfeeding population.
- Formula feeding was not associated with increased mortality risk overall, or after controlling for or stratifying by infant HIV-1–infection status.
- Formula feeding was not associated with increased 2-year incidence of diarrhea, pneumonia, malnutrition, or any other measured morbidity.
- Breastfeeding conferred better nutritional status, particularly during the first 6 months of life.
- Formula feeding was associated with significantly better HIV-1–free survival at 2 years; ie, children in the formula group were more likely to be alive and HIV-1 uninfected than those in the breastfeeding group. To us, this composite study outcome measure is the critical one.
- Mothers in the breastfeeding group had a 3-fold higher mortality risk.

From these key findings, we concluded that formula feeding was associated with better health outcome for HIV-1–infected mothers and their children than breastfeeding in our trial.

Although formula feeding provided clear benefits, it also conferred some risks, including higher incidence of dehydration and current diarrhea during the first 3 months (but not subsequently), poorer nutritional status, especially during the first 6 months, and a higher incidence of death due to sepsis. Thus, we advocate careful follow-up of formula fed infants with attention to these potential complications.

The 30% noncompliance rate in the formula feeding group would have the effect of attenuating measured differences toward the null. We presented a mortality analysis based on true feeding modality but found very similar results as those from an intent-to-treat analysis.

Infant HIV-1–infection status for most children in our trial was based on viral DNA detection rather than enzyme-linked immunosorbent assays. Precise timing of HIV-1 infection may be difficult to determine, hence our choice of a randomized clinical trial design.

Our findings contradict those of previous observational studies evaluating the risks associated with use of replacement feeds. We raised the possibility that breastmilk of HIV-1–infected women may be lacking in protective factors because of maternal immunosuppression.

Both Kent and Brussel et al raise the issue of mixed feeding. Our trial was not designed to determine the risk of breastmilk transmission in mixed vs exclusively breastfed infants. We encourage further research to address this issue.

We agree with several important points made by Dr Nogueira. We encourage caution in interpreting results from observational studies of feeding method and HIV-1 transmission because feeding practices are often influenced by maternal health status, and hence results are subject to confounding. Nogueira mentions the challenge of educating women to change their feeding practices, specifically with regards to the time of introduction of weaning foods, a point that has not received adequate attention.

There is no question that breastfeeding is the optimal form of nutrition for young infants globally. However, in the context of HIV-1 infection in the mother, replacement feeding is the best way to prevent breastmilk transmission. We acknowledge that this may not be a suitable option for many HIV-1–infected women in poor communities but emphasize that for women with safe water supplies and access to health education, formula feeding can be a viable and safe strategy to prevent pediatric HIV-1 infections.

Dorothy Mbori-Ngacha, MBChB, MPH
Ruth Nduati, MBChB, MPH
University of Nairobi
Nairobi, Kenya
Grace John-Stewart, MD, PhD
Barbra Richardson, PhD
Joan Kreiss, MD, MSPH
University of Washington
Seattle

In Reply: As Dr Nogueira states, the study by Mbori-Ngacha et al[1] was well designed and carefully implemented and analyzed. Our comments about the trial's results reinforced some of the conclusions made by the authors themselves. The authors indicated that their results were not necessarily generalizable to all women and represented a best-case scenario. All

women had access to clean water, extensive health education, and medical care and close follow-up of their infants. For women in countries such as Brazil, Thailand, South Africa, and the subset of women in all resource-poor settings who have similar access, the findings of Mbori-Ngacha et al are reassuring. Formula feeding can decrease the rate of HIV transmission and can likely be done with minimal risk to the infant under these circumstances. However, this study does not establish that access to and use of formula is indeed safe and effective nor desired by all women in developing countries.

Dr Kent and Ms Brussels and colleagues raise concerns regarding the conclusions reached by Mbori-Ngacha et al. As we indicated in our Editorial, we agree with the suggestion that the study's results be interpreted with caution. While interesting and potentially of great importance, the lack of significant excess morbidity and mortality among formula-fed infants was surprising and warrants additional study to see if similar results are observed in settings where the risks of alternative feeding may be greater.

Dr Nogueira's comments reflect the ongoing dilemma raised by the risk of HIV transmission through breastfeeding. Recommendations regarding breastfeeding for an HIV-infected woman are of necessity based on her individual risk-benefit ratio. In resource poor areas where infant mortality rates may exceed 100 deaths/1000 live births, the risks of alternative feeding may outweigh the risk of HIV transmission through breastfeeding. In such settings HIV-infected women have fewer infant feeding options than women in countries with more resources. Support of breastfeeding among HIV-infected women in resource poor settings who cannot safely provide or choose not to use alternative feeding strategies does not reflect a double standard. Recommendations regarding infant feeding practices should be based on an individual's known risks and benefits; that the same recommendation cannot be made for everyone reflects global health inequities. The fact that HIV infected women will continue to breast feed their infants is a reality, and the obligation of health care workers is to try to make whatever infant feeding option a mother chooses as safe as possible.

Laura Guay, MD
Departments of Pathology and Pediatrics
Johns Hopkins University School of Medicine
Baltimore, Md

Andrea Ruff, MD
Department of International Health
Johns Hopkins University Bloomberg School of Public Health
Department of Pediatrics
Johns Hopkins University School of Medicine
Baltimore

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1. Mbori-Ngacha D, Nduati R, Grace J, et al. Morbidity and mortality in breastfed and formula-fed infants of HIV-1–infected women: a randomized clinical trial. *JAMA*. 2001;286:2413-2420.

Physicians' Feelings About Themselves and Their Patients

To the Editor: In their discussion of the inner life of physicians, Dr Meier and colleagues[1] propose a medical model to address emotionally sensitive issues that most physicians keep secret. The medical model that I use to understand such issues is that of posttraumatic stress disorder (PTSD), which is defined as a set of typical symptoms that develop after a person sees, is involved in, or hears of an "extreme traumatic stressor."[2] Although PTSD has been described as a consequence of rape, war, bombings, or other obvious overt traumas,[3] it is usually not considered a result of medical training.

I believe that most physicians have PTSD and that the resulting feeling that physicians ignore most is toxic shame. Shame has been defined as the failure to live up to one's own expectations.[4] I define shame as the healthy sense that one is limited and toxic shame as the belief that one is defective.[5] Toxic shame has its roots in PTSD.

During their training, physicians experience both physical (80- to 100-hour work weeks) and emotional (shaming by professors and supervising house staff) abuse. Once in practice, patient care "retriggers" the toxic fear, loneliness, pain, anger, and shame physicians experienced in training. I believe these extreme feelings are related to PTSD. Although these feelings may be "normal," they certainly are not healthy if left untreated.

Physicians survive PTSD through isolating in work, hiding their feelings, and deceiving others and themselves. Isolation then promotes accepted mood-altering codependent behaviors of excessive attempts to please others, intellectualization, workaholism, secret keeping, and perfectionism. Less acceptable but tolerated behaviors include passive-aggressive failure to perform needed duties (eg, finishing their medical records) or shaming of paraprofessional personnel (eg, condescending anger toward nursing staff). Only when end-stage behaviors occur (such as crossing romantic boundaries with patients or overt drug addiction) do colleagues and others intervene.

I believe the solution requires that medical schools, psychiatrists, and hospital administrators embrace the medical model of PTSD in evaluating and intervening in physician mental health problems. Unless taught these tenets, physicians cannot fully assess their feelings or confront and support others in their own struggles. Unless educated about these potential problems, hospital administrators and medical schools will not see their role in perpetrating or enabling the maladaptive behaviors and learn how to confront them effectively.

James S. Kennedy, MD, CCS
Department of Medicine
Vanderbilt University
Nashville, Tenn

1. Meier DE, Back AL, Morrison RS. The inner life of physicians and care of the seriously ill. *JAMA*. 2001;286:3007-3014.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, DC: American Psychiatric Association; 1994.

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To the Editor: In emphasizing physicians' reactions to the care of seriously ill patients, Dr Meier and colleagues[1] may have overlooked their reactions to conditions that may not be life-threatening but nonetheless significantly affect the quality of those patients' lives. Spinal cord injuries are perhaps the most obvious of these conditions. It is important for physicians to recognize that caring for patients with any condition with the potential for even partially limiting activities important to the individual may provide reminders of the physician's own vulnerability. This can put the physician at risk for feelings that, unless recognized, could impair patient care.

Simon Auster, MD, JD
Departments of Family Medicine and Psychiatry
F. Edward Hébert School of Medicine
Uniformed Services University of the Health Sciences
Bethesda, Md

Disclaimer: The opinion expressed herein is that of the author and does not necessarily reflect that of the Department of Defense.

1. Meier DE, Back AL, Morrison RS. The inner life of physicians and care of the seriously ill. *JAMA*. 2001;286:3007-3014.

To the Editor: Dr Meier and colleagues[1] describe a model for assisting physicians to maximize their patients' and their own well-being. Their approach identifies risk factors, signs and symptoms, differential diagnosis, and intervention strategies for physicians to use as a guide toward identifying and addressing emotional distress. Yet application of these standard medical principles to emotional dynamics does not allow for deeper exploration of emotion. The medicalization of emotion in this context may, for some, create yet another wall for physicians to stand behind when emotions threaten to overwhelm them. In other words, use of a medical approach may actually strengthen the barriers this model seeks to alleviate.

Aside from the limitation of its medical basis (which Meier et al recognize), the model does not appear to be comprehensive enough to allow physicians to achieve substantial self-knowledge of emotions and self-awareness of behaviors applicable to various situations. Although Meier et al suggest that self-monitoring be a routine skill, what seems to be called for is a broader acceptance in medicine of the humanness of physicians.

Recognition of what it really means to be a physician—the sense of power or powerlessness, of connection and disconnection—is both an attitude and a skill that may be imparted to physicians over the course of their medical education and practice through some deviance from strict medical model standards. Pervasive and routine emphasis on self-knowledge, self-awareness, and compassion can complement medical protocols. Mechanisms such as support seminars and grand rounds may help create a supportive environment wherein the open discussion of emotions is not preempted by a rebound to the familiar and comfortable, yet emotionally unchallenging, technicalities of patient care. The inner life of individual physicians should, to some extent, be brought into the outer life of physicians as a collective.

Dena Schulman-Green, PhD
Center for Excellence in Chronic Illness Care
Yale University
New Haven, Conn

1. Meier DE, Back AL, Morrison RS. The inner life of physicians and care of the seriously ill. *JAMA*. 2001;286:3007-3014.

In Reply: These letters reflect a range of concerns about the impact of the inner emotional lives of physicians on the care of their patients. Dr Kennedy likens the sequelae of the trauma of medical education to PTSD. Dr Auster argues that phenomena similar to those described among physicians caring for persons with life-threatening illness also affect physicians' care for patients with chronic degenerative disorders or disabilities. Dr Schulman-Green believes that medical educational and community norms should change to integrate the recognition of the role that unexamined feelings can have on both physician and patient. Judging by these letters, our article seems to have stimulated dialogue on the responsibility of the profession to acknowledge that physicians are people too, with feelings that may affect care of patients. If the self-evidence of this observation is accepted by medical educators, some of the suggestions offered by these writers may find their way into the curriculum both for physicians in training as well as those already in practice.

Diane E. Meier, MD
Department of Geriatrics and Adult Development
Mount Sinai School of Medicine
New York, NY
Anthony L. Back, MD
Department of Medicine
University of Washington School of Medicine
Seattle
R. Sean Morrison, MD
Department of Geriatrics and Adult Development
Mount Sinai School of Medicine
New York

RESEARCH LETTER

Molecular Analysis of Early Postvaccine Mumps-like Disease in Italian Military Recruits

To the Editor: Italian military recruits have received mandatory mumps vaccination by Urabe Am9 strain since 1998. A previous study[1] found that, in 1999, 37 episodes of mumps-like disease were found in recipients of the vaccine, and that 35 of these occurred within 1 month of immunization. To assess whether these cases were due to some expected residual virulence of the live attenuated Urabe Am9 mumps strain, we

analyzed saliva samples from recruits who developed mumps-like disease within 1 month of vaccination.

Methods. After informed consent, saliva samples were collected from 20 military recruits who had developed mumps-like disease and from 14 randomly selected asymptomatic recruits 1 month following vaccination. For positive amplification control a commercial Jeryl Linn vaccine strain was used (M-M-R-II, Aventis Pasteur MSD, Lyon, France). Viral RNA was extracted according to the manufacturer's instructions (Machery-Nagel, Duren, Germany), retrotranscribed with avian myeloblastosis virus enzyme (Roche, Basel, Switzerland) and amplified by nested polymerase chain reaction.[2] Amplified fragments were first purified, then sequenced using a BigDye Terminator kit in a 377ABI sequencer (Applied Biosystems, Foster City, Calif). The obtained sequences, together with the consensus sequence of Urabe Am9,[3] have been aligned by the CLUSTALW tool (available at: http://www2.ebi.ac.uk/clustalw/).

Results. Fifteen of the 20 saliva samples from vaccinated subjects with mumps-like disease were positive for mumps RNA, whereas all saliva samples from asymptomatic controls were negative. The positive samples were sequenced and all of them completely overlapped the reference consensus sequence of Urabe Am9.

Comment. Wild mumps virus genotypes A and C are predominant in Europe, whereas genotype B is nearly absent.[4] This information, together with the results of our study, confirms that Urabe Am9 vaccine (a B genotype strain) can be associated with early mumps-like disease, which, therefore, may be considered as a possible vaccine-induced adverse effect. This finding is not unexpected and is shared by all mumps live-attenuated vaccines.[5]

In light of these molecular data, our previous conclusion[1] that Urabe Am9 is 70% effective may actually be too low, as the efficacy of the Urabe Am9 vaccine against wild-virus infections could be underestimated if vaccine-associated cases are included. However, Cohen et al,[2] using a different vaccine strain, found that natural mumps disease can occur 16 days after vaccination. Thus, for subjects for whom molecular data are not available, the possibility of a coincidental infection with wild-type mumps virus cannot be completely ruled out.

Florigio Lista, MD
Giovanni Faggioni, PhD
Mario Stefano Peragallo, MD
Francesco Tontoli, MD
Ispettorato Logistico dell'Esercito
Centro Studi e Ricerche di Sanità e Veterinaria
Rome, Italy

Antonio Stella, MD
Piero Salvatori, MD
Michele Pusino, MD
Marlo Alberto Germani, MD
Vito Contreas, MD
Ispettorato Logistico dell'Esercito
Policlinico Militare di Roma
Rome

Raffaele D'Amelio, MD
Aeronautica Militare, Comando Logistico, Servizio Sanitario
Università di Roma "La Sapienza"
II Facoltà di Medicina e Chirurgia
Rome

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