

The Bare Bones of Sex: Part 1—Sex and Gender

Here are some curious facts about bones. They can tell us about the kinds of physical labor an individual has performed over a lifetime and about sustained physical trauma. They get thinner or thicker (on average in a population) in different historical periods and in response to different colonial regimes (Molleson 1994; Larsen 1998). They can indicate class, race, and sex (or is it gender—wait and see). We can measure their mineral density and whether on average someone is likely to fracture a limb but not whether a particular individual with a particular density will do so. A bone may break more easily even when its mineral density remains constant (Peacock et al. 2002).¹

Culture shapes bones. For example, urban ultraorthodox Jewish adolescents have lowered physical activity, less exposure to sunlight, and drink less milk than their more secular counterparts. They also have greatly decreased mineral density in the vertebrae of their lower backs, that is, the lumbar vertebrae (Taha et al. 2001). Chinese women who work daily in the fields have increased bone mineral content and density. The degree of increase correlates with the amount of time spent in physical activity (Hu et al. 1994); weightlessness in space flight leads to bone loss (Skerry 2000); gymnastics training in young women ages seventeen to twenty-seven correlates with increased bone density despite bone resorption caused by total lack of menstruation (Robinson et al. 1995). Consider also some recent demographic trends: in Europe during the past thirty years, the number of vertebral fractures has increased three- to fourfold for women and more than fourfold for men (Mosekilde 2000); in some

Thanks to the members of the Pembroke Seminar on Theories of Embodiment for a wonderful year of thinking about the process of body making and for their thoughtful response to an earlier draft of this essay. Credit for the title goes to Greg Downey. Thanks also to anonymous reviewers from *Signs* for making me sharpen some of the arguments.

¹ Munro Peacock et al. write: “The pathogenesis of a fragility fracture almost always involves trauma and is not necessarily associated with reduced bone mass. Thus, fragility fracture should neither be used synonymously nor interchangeably as a phenotype for osteoporosis” (2002, 303).

groups the relative proportions of different parts of the skeleton have changed in recent generations.² (See also table 1.)

What are we to make of reports that African Americans have greater peak bone densities than Caucasian Americans (Aloia et al. 1996; Gilsanz et al. 1998),³ although this difference may not hold when one compares Africans to British Caucasians (Dibba et al. 1999), or that white women and white men break their hips more often than black women and black men (Kellie and Brody 1990)?⁴ How do we interpret reports that Caucasian men have a lifetime fracture risk of 13–25 percent compared with Caucasian women’s lifetime risk of 50 percent even though once peak bone mass is attained men and women lose bone at the same rate (Seeman 1997, 1998; NIH Consensus Statement Online 2000)?

Such curious facts raise perplexing questions. Why have bones become more breakable in certain populations? What does it mean to say that a lifestyle behavior such as exercise, diet, drinking, or smoking is a risk factor for osteoporosis? Why do we screen large numbers of women for bone density even though this information does not tell us whether an individual woman will break a bone?⁵ Why was a major public policy statement on women’s health unable to offer a coherent account of sex (or is it gender?) differences in bone health over the life cycle (Wizemann and Pardue 2001)? Why, if bone fragility is so often considered to be a sex-related trait, do so few studies examine the relationships among childbirth, lactation, and bone development (Sowers 1996; Glock, Shanahan, and McGowan 2000)?

Such curious facts and perplexing questions challenge both feminist and biomedical theory. If “facts” about biology and “facts” about culture are all in a muddle, perhaps the nature/nurture dualism, a mainstay of

² For example, sitting height reflects trunk length (vertebral height) vs. standing height, which reflects the length of the leg bones. These can change independently of one another. Thus height increases can result from changes in long bone length, vertebral height, or both. See Meredith 1978; Tanner et al. 1982; Malina, Brown, and Zavaleta 1987; Balthazart, Tlemçani, and Ball 1996; Seeman 1997.

³ The use of racial terms such as *Caucasian* and others in this article is fraught. But for the duration of this article I will use the terms as they appear in the sources I cite, leaving an analysis of this problematic terminology to future publications, e.g., Fausto-Sterling 2004.

⁴ Since a number of studies show no sex difference in hip fracture incidence between African American men and women, the “well-known” gender difference in bone fragility may really only be about white women. As so often happens, the word *gender* excludes women of color (Farmer et al. 1984).

⁵ Peacock et al. write, “Key bone phenotypes involved in fracture risk relate not only to bone mass but also to bone structure, bone loss, and possibly bone turnover” (2002, 306).

feminist theory, is not working as it should. Perhaps, too, parsing medical problems into biological (or genetic or hormonal) components in opposition to cultural or lifestyle factors has outlived its usefulness for biomedical theory. I propose that already well-developed dynamic systems theories can provide a better understanding of how social categories act on bone production. Such a framework, especially if it borrows from a second analytic trend called “life course analysis of chronic disease epidemiology” (Kuh and Ben-Shlomo 1997; Ben-Shlomo and Kuh 2002; Kuh and Hardy 2002), can improve our approaches to public health policy, prediction of individual health conditions, and the treatment of individuals with unhealthy bones.⁶ To see why we should follow new roads, I consider gender, examining where we—feminist theorists and medical scientists—have recently been. In the second part of this study (Fausto-Sterling in preparation) I will engage with current discussions of biology, race, and medicine to explore claims about racial difference in bone structure and function.

Sex and gender (again)

For centuries, scholars, physicians, and laypeople in the United States and Western Europe used biological models to explain the different social, legal, and political statuses of men and women and people of different hues.⁷ When the feminist second wave burst onto the political arena in the early 1970s, we made the theoretical claim that sex differs from gender and that social institutions produce observed social differences between men and women (Rubin 1975). Feminists assigned biological (especially reproductive) differences to the word *sex* and gave to *gender* all other differences.

“Sex,” however, has become the Achilles’ heel of 1970s feminism. We relegated it to the domain of biology and medicine, and biologists and medical scientists have spent the past thirty years expanding it into arenas we firmly believed to belong to our ally gender. Hormones, we learn (once more), cause naturally more assertive men to reach the top in the workplace (Dabbs and Dabbs 2001). Rape is a behavior that can be changed only with the greatest difficulty because it is wired somehow into men’s brains (Thornhill and Palmer 2001). The relative size of eggs and sperm dictate that men are naturally polygamous and women naturally monogamous. And more. (See Zuk 2002; Travis 2003 for a critique of

⁶ I am grateful to Peter Taylor for insisting that I read the work in life-course analysis.

⁷ Stepan 1982; Russett 1989; Hubbard 1990; Fausto-Sterling 1992.

Table 1. Culture Changes Bones

Observation	Reference
Vertebral BMD (gm/cm ²) increased in young women during an eight-month program of running or weight-training compared with untrained controls.	Snow-Harter et al. 1992
Two years of aerobics and weight training enhances BMD in young women; gymnastics training improves mechanical competence of skeleton in boys.	Friedlander et al. 1995; Daly et al. 1999
Intensive tennis playing increases bone mineral content, BMAD, and thickness of the humerus of the racket arm; the effect is especially noticeable in players who began at ages 9–10, and the effect is there for both males and females. Later-in-life start-up (29 years) resulted in more marginal effects.	Jones et al. 1977; Haapasalo et al. 1996
Cross-country skiers who train year-round have site-specific increases in BMD (study on females age ~16).	Pettersson et al. 2000
In late-adolescent women, weight-bearing activities are important for determining bone density; high-impact activities modify bone width due to increased muscle strength and lean body mass; lean mass, fat mass, weight, BMI, years of menstruation, and type of physical activity explained 81.6 percent of bone variation.	Soderman et al. 2000
In Japanese women with a genetic variant that impairs vitamin D receptor, exercise, vitamin D, and calcium intake can increase BMD.	Fujita et al. 1999
Long-term exercise improves balance in older osteoarthritic adults (fewer falls).	Messier et al. 2000
In a longitudinal study of youth ages 13–27, maintaining at least an average weight was the best predictor of high BMD in females.	Welton et al. 1994
Premenopausal, but not postmenopausal, women respond to a regime of vertical jumping exercises with increased BMD in their femurs.	Bassey and Ramsdale 1994; Bassey et al. 1998
Physical activity and muscle strength independently predict BMD in total body and in the proximal femur in young men.	Nordstrom, Nordstrom, and Lorentzan 1997
Amateur sports at ages 11–30 improves bone density in a site- or stress-specific fashion (study done on young men).	Nordstrom et al. 1996; Morel et al. 2001
Prepubertal Asian Canadian boys have lowered femoral neck BMC and BMD, ingest 41 percent less calcium, and are 15 percent less active than Caucasian Canadian boys.	McKay et al. 2000

Table 1. (Continued)

Observation	Reference
Over three years, men and women over age 65 receiving calcium and vitamin D supplements show less bone loss in the femur and spine and a lower incidence of nonvertebral fractures.	Dawson-Hughes et al. 1997
Ninety percent of adolescent girls and 50 percent of adolescent boys consume less than optimal amounts of dietary calcium.	Bachrach 2001
Fifty percent of 12- to 21-year-olds exercise vigorously and regularly; 25 percent report no vigorous physical activity.	Bachrach 2001
Alcohol consumption correlates with higher BMD, smoking with lower BMD.	Siris et al. 2001
Anorexia nervosa injures bone development and maintenance.	Muñoz and Argente 2002
In the twentieth century, American youth of African, European, and Japanese ancestry increased in height due to changes in sitting height and increase in lower limb length.	Meredith 1978

Note: BMD = bone mineral density, BMAD = bone mineral apparent density (the measure is independent of size), BMI = body mass index, and BMC = bone mineral content.

these claims.) Feminist scholars have two choices in response to this spreading oil spill of sex. Either we can contest each claim, one at a time, doing what Susan Oyama calls “hauling the theoretical body back and forth across the sex/gender border” (2000a, 190), or, as I choose to do here, we can reconsider the 1970s theoretical account of sex and gender.

In thinking about both gender and race, feminists must accept the body as simultaneously composed of genes, hormones, cells, and organs—all of which influence health and behavior—and of culture and history (Verbrugge 1997). As a biologist, I focus on what it might mean to claim that our bodies physically imbibe culture. How does experience shape the very bones that support us?⁸ Can we find a way to talk about the body without ceding it to those who would fix it as a naturally determined object existing outside of politics, culture, and social change? This is a project already well under way, not only in feminist theoretical circles but in epidemiology, medical sociology, and anthropology as well.

⁸ I use the term *experience* rather than the term *environment* here to refer to functional activity. For more detail see Gottlieb, Whalen, and Lickliter 1998.

Embodiment merges biology and culture

During the 1990s, feminist reconsideration of the sex/gender problem moved into full swing.⁹ Early in the decade Judith Butler argued compellingly for the importance of reclaiming the term *sex* for feminist inquiry but did not delve into the nuts and bolts of how sex and gender materialize in the body. Philosopher Elizabeth Grosz (1994) claimed that sex is neither fixed nor given. In drawing on philosophers such as Maurice Merleau-Ponty (1962) and Alfred North Whitehead ([1929] 1978), Grosz differentiates herself from Butler, holding that materiality is “primordial, not merely the effect of power” (Alcoff 2000, 858). Primordial materiality, however, does not mean that purely biological accounts of human development—no matter how intricate their stories of cellular function—can explain the emergence of lived and differently gendered realities.¹⁰

Psychologist Elizabeth Wilson offers one of the most interesting and far-reaching critiques of feminist attempts to reclaim the body (Martin 1997; Wilson 1998, 1999). Reaching back to Sigmund Freud’s work on hysteria, Wilson emerges with a new purchase on biology itself. Reiterating the varied symptoms produced by psychic trauma (blindness, localized pain, loss of smell, paralysis), she focuses on the “bio-logic” of these physical manifestations (1999). “The neurology, physiology, or biochemistry of hysterical symptomology,” she writes, “can be disregarded only in a theoretical milieu that takes certain modes of materiality to be inert” (1999, 10). She suggests that just as “culture,” “signification,” or “sociality” contribute to the production of complex bodily responses, “biology itself” ought to be investigated as a “site of . . . complex ontological accomplishment” (10). Such investigation, Wilson argues, opens the door for a fundamental reexamination of biomedical analyses of sex differences in physiology and disease patterns. The idea of embodiment as a dynamic system of biocultural formation reaches beyond discussions of gender (e.g., Csordas 1990; Ingold 1998; Williams and Bendelow 1998).¹¹

Efforts to reincorporate the body into social theory also come from the field of disability studies. Here too an emphasis on the social con-

⁹ Butler 1990, 1993; Gatens 1996; Kirby 1997; Birke 1999.

¹⁰ The “rediscovery” of phenomenology and its application to gendered body image remains a fruitful arena of feminist body theory, e.g., Weiss 1999.

¹¹ Although Thomas J. Csordas (1999) suggests that cultural phenomenological analyses transform understandings of both biology and culture, he is more concerned with how the body changes culture than vice versa. For a different anthropological point of view, see Ingold 1998.

struction of disability has been enormously productive. Yet several authors have broached the limitations of an exclusively constructivist approach. At least two different types of critique parallel and foreshadow possible feminist approaches to a reconsideration of the body. The first demands that we recognize the material constraints on the disabled body in its variable forms and that we integrate that recognition into theory (Williams and Busby 2000). The second, more radical move is to suggest that “the disabled body changes the process of representation itself” (Siebers 2001, 738). This latter approach offers a rich resource for feminist theories of representation and another possible entry point into the analysis of materiality in actual, lived-in bodies (see also Schriempf 2001).

Sex and gender in the world of biology and medicine

In contrast to these new feminist explorations of the body, in the field of medicine a more limited view of sex differences prevails. Consider a recent report on sex differences issued by the National Institute of Medicine and, more broadly, the professional movement called “gender-based medicine” promoted by the Society for Women’s Health Research (SWHR). The SWHR describes itself as “the nation’s only not-for-profit organization whose sole mission is to improve the health of women through research. . . . The Society . . . encourages the study of sex differences that may affect the prevention, diagnosis and treatment of disease and promotes the inclusion of women in medical research studies” (Schachter 2001, 29).¹² The society lobbies Congress, sponsors research conferences, and publishes a peer-reviewed academic journal, the *Journal of Women’s Health and Gender-Based Medicine*.

A traditional biomedical model of health and disease provides the intellectual framework for the research conferences (Krieger and Zierler 1995). Although much of the research publicized through such conferences seems strictly to deal with *sex* in the 1970s feminist meaning of the word, sex sometimes strays into arenas that traditional feminists claim for gender. Consider a presentation that was said to provide evidence that prenatal testosterone exposure affects which toys little girls and boys prefer

¹² Since the society receives both foundation and pharmaceutical company funding, its claim to independence requires scrutiny. The Sex and Gene Expression conferences were funded by Aventis Pharmaceuticals as well as private foundations. Industry and mainstream medical care sponsorship does not unethically direct work, but it limits the permissible ontological and epistemological approaches to the study of women’s health and sex differences.

to play with (Berenbaum 2001). Working within a 1970s definition of the sex/gender dualism, the author of this study logically extends the term *sex* into the realm of human behavior.

For those familiar with contemporary feminist theory, it might seem that the large number of biological psychologists who follow similar research programs and the biomedical researchers interested in tracking down all of the medically interesting differences between men and women live in a time warp. But members of the feminist medical establishment, that is, those researchers and physicians for whom the activities and programs of the SWHR make eminent sense, see themselves perched on the forward edge of a nascent movement to bring gender equity to the health-care system. These feminists work outside of an intellectual milieu that would permit the more revolutionary task proposed by Grosz and Wilson, among others, that of contesting not only “the domination of the body by biological terms but also [contesting] the terms of biology itself” (Grosz 1994, 20).

Within medicine there is a lot of confusion about the terms *sex* and *gender*. Many medical texts use the terms interchangeably, while some scientists apply the term *gender* to the study of nonhuman animals, a problem also debated in the primary biological literature (Pearson 1996; Thomas et al. 2000). Lack of consistent usage promotes confusion among scientists, policy makers, and the general public, in effect foreclosing any space for the analysis of social causes of differences in health outcomes between men and women (Krieger 2003).

Helen Keane and Marsha Rosengarten (2002) have explored the body as a dynamic process out of which gender emerges. In a first example they examine the significance of anabolic steroid use on the alteration of sexed bodies, concluding that “the hormonal body is always in process rather than fixed” (269); they further explore the notion of sex/gender fixity through a discussion of organ transplantation between XX and XY individuals. Finally, they examine “the biological *as* a field of transformations, as active, ‘literate matter’ as well as an effect *of* mediation and intervention” (275). I have chosen bone development—an area often accepted as an irrefutable site of sex difference—to examine Keane and Rosengarten’s formulation. First, to what extent can we understand bone formation as an effect of culture rather than a passive unfolding of biology? Second, can we use dynamic (developmental) systems to ask better research questions and to formulate better public-health responses to bone disease?

Why bones?

Bones are eloquent. Archaeologists read old bone texts to find out how prehistoric peoples lived and worked. A hyperflexed and damaged big toe, a bony growth on the femur, the knee, or the vertebrae, for example, tell bioarchaeologist Theya Molleson that women in a Near Eastern agricultural community routinely ground grain on all fours, grasping a stone grinder with their hands and pushing back and forth on a saddle-shaped stone. The bones of these neolithic people bear evidence of a gendered division of labor, culture, and biology intertwined (Molleson 1994).¹³

Given that modern forensic pathologists also use bones to learn about how people live and die, it seems odd that a report from the National Institute of Medicine, presented as a state-of-the-art account of gender and medicine, deals only superficially with the sexual differentiation of bone disease (Wizeman and Pardue 2001).¹⁴ In a brief three pages on osteoporosis, the monograph cites dramatic statistics on the frequency of osteoporosis in European and Caucasian American women and the dangers of the condition. The report offers a laundry list of factors believed to affect bone health. Jumbled together, with no attempt to understand their interrelationships or their joint, cumulative contributions to bone development and loss, are hormones, diet, exercise, genetic background, vitamin D production, and the bone-destroying effects of drugs such as cortisone, tobacco, and alcohol. In an anemic end-of-chapter recommendation the authors urge researchers to control for all of the above factors as they design their research studies. Indeed, failure to engage the task of formulating new approaches to biology prevented them from making a stronger analysis.

But osteoporosis is a condition that reveals all of the problems of defining sex apart from gender. A close reading of the osteoporosis literature further reveals the difficulties of adding the variable of race to the mix (a point I will develop in a forthcoming paper [Fausto-Sterling in preparation]) while also exemplifying the claim that disease states are socially produced, both by rhetoric and measurement (e.g., Petersen 1998) and

¹³ Perhaps because the field of archaeology is still struggling to bring gender into the fold, its practitioners often insist on the centrality of the sex/gender distinction. Yet their own conclusions undermine this dualism, precisely because they use a biological product, bone, to draw conclusions about culture and behavior (Ehrenberg 1989; Gero and Conkey 1991; Wright 1996; Armelagos 1998).

¹⁴ The validity of using bones to identify race is contested (Goodman 1997).

by the manner in which cultural practice shapes the very bones in our bodies (Krieger and Zierler 1995).

Of bones and (wo)men

The accuracy of the claim that osteoporosis occurs four times more frequently in women than in men (Glock, Shanahan, and McGowan 2000) depends on how we define osteoporosis, in which human populations (and historical periods) we gather statistics, and what portions of the life cycle we compare. The NIH (2000) defines osteoporosis as a skeletal disorder in which weakened bones increase the risk of fracture. When osteoporosis first wandered onto the medical radar screen, the only signal that a person suffered from it was a bone fracture. Post hoc, a doctor could examine a person with a fracture either using a biopsy to look at the structural competence of the bone or by assessing bone density.

If one looks at lifetime risks for fracture, contemporary Caucasian men range from 13 to 25 percent (Bilezikian, Kurkland, and Rosen 1999) while Caucasian women (who also live longer) have a 50 percent risk. But not all fractures result from osteoporosis. One study looked at fracture incidence in men and women at different ages and found that between the ages of five and forty-five men break more limbs than women.¹⁵ The breaks, however, result from significant work- and sports-related trauma suffered by healthy bones. After the age of fifty, women break their bones more often than men, although after seventy years of age men do their best to catch up (Melton 1988).

The most commonly used medical standard for a diagnosis of osteoporosis no longer depends on broken bones. With the advent of machines called densitometers used to measure bone mineral density (of which more in a moment), the World Health Organization (WHO) developed a new “operational” definition: a woman has osteoporosis if her bone mineral density measures 2.5 times the standard deviation below a peak reference standard for young (white) women. The densitometer manufacturer usually provides the reference data to a screening facility (Seeman 1998), and thus rarely, if ever, do assessments of osteoporosis reflect what Margaret

¹⁵ This study (cited in Melton 1988) dates from 1979, and it seems likely that subsequent cultural changes have led to different patterns of breakage; fracture incidence is a moving target.

Lock calls “local biologies” (Lock 1998, 39).¹⁶ With the WHO definition, the prevalence of osteoporosis for white women is 18 percent, although there is not necessarily associated pathology, since now, by definition, one can “get” or “have” osteoporosis without ever having a broken bone. The WHO definition is controversial, since bone mineral density (BMD, or grams/cm²) accounts for approximately 70 percent of bone strength, while the other 30 percent derives from the internal structure of bone and overall bone size. And while women with lower bone density are 2.5 times more likely to experience a hip fracture than women with high bone densities, high risks of hip fracture emerge even in women with high bone densities when five or more other risk factors are present (Cummings et al. 1995).¹⁷ Furthermore, it is hard to know how to apply the criterion, based on a baseline of young white women, to men, children, and members of other ethnic groups. To make matters worse, there is a lack of standardization between instruments and sites at which measurements are taken.¹⁸ Thus it comes as no surprise that “controversy exists among experts regarding the continued use of this [WHO] diagnostic criterion” (NIH Consensus Statement Online 2000, 3).

There is a complicated mixture at play. First, osteoporosis—whether defined as fractures or bone density—is on the rise, even when the increased age of a population is taken into account (Mosekilde 2000). At the same time, it is hard to assess the danger of osteoporosis, in part due to drug company–sponsored “public awareness” campaigns. For example, in preparation for the sales campaign for its new drug, Fosamax, Merck Pharmaceuticals gave a large osteoporosis education grant to the National Osteoporosis Foundation to educate older women about the dangers of osteoporosis (Tanouye 1995).¹⁹ Merck also directly addressed consumers

¹⁶ Local biologies reflect local differences in biology. For example, hot flashes are far less frequent in Japan than in the United States, possibly for reasons pertaining to diet. The normalization question here is: Is it best to compare a population to its own group or some group with similar environmental and genetic histories, or to some outgroup standard?

¹⁷ These factors include: a mother having broken her hip, especially before age eighty; height at age twenty-five (taller women are more likely to break hips); extreme thinness; sedentary lifestyle; poor vision; high pulse rate; the use of certain drugs; etc.

¹⁸ One researcher states: “I think what is also of note, is that the between-center differences are greater than between-sex differences within certain centers” (Lips 1997, 95).

¹⁹ Fosamax seems to be able to prevent further bone loss in people who are losing bone and to build back lost bone at least in the hip and spine. In discussing Merck’s campaign, I do not argue that the drug is useless (in fact, I am taking it!), merely (!) that drug companies play an important role in the creation of new “disease” and profit as a result.

with television ads contrasting frail, pain-wracked older women with lively, attractive seniors, implying the urgent need for older women to use Fosamax (Fugh-Berman, Pearson, Allina, Zones, Worcester, and Whatley 2002).

Mass marketing a new drug, however, requires more than a public awareness campaign. There must also be an easy, relatively inexpensive method of diagnosis. Here the slippage between the new technological measure—bone density—and the old definition of actual fractures and direct assessment of bone structure looms large. Merck promoted affordable bone density testing even before it put Fosamax on the market. The company bought an equipment manufacturing company and ramped up its production of bone density machines while at the same time helping consumers find screening locations by giving a grant to the National Osteoporosis Foundation to push a toll-free number that consumers (presumably alarmed by the Merck TV ads) could call to find a bone density screener in a locale near them (Tanouye 1995; Fugh-Berman, Pearson, Allina, Zones, Worcester, and Whatley 2002).

The availability of a simple technological measure for osteoporosis also made scientific research easier and cheaper. The majority of the thousands upon thousands of research papers on osteoporosis published in the ten years from 1995 to 2005 use BMD as a proxy for osteoporosis. This is true despite a critical scientific literature that insists that the more expensive volumetric measure (grams/cm³) more accurately measures bone strength and that knowledge of internal bone structure (bone histomorphometry) provides essential information for understanding the actual risk of fracture (Meunier 1988).²⁰ The explosion of knowledge about osteoporosis codifies a new disorder, still called osteoporosis but sporting a newly simplified account of bone health and disease.²¹ Ego Seeman (1997) laments the

²⁰ “An association between the change in areal bone density and the change in fracture rates has never been documented” (Seeman 1997, 517). According to the NIH Consensus Statement Online: “Currently there is no accurate measure of overall bone strength” (2000, 5). But BMD is often used as a proxy. The National Women’s Health Network cites the pitfalls of using BMD to predict future fractures (Fugh-Berman, Pearson, Allina, Zones, Worcester, Whatley, Massion, et al. 2002), but others cite a strong association between BMD and fracture rate (e.g., Melton et al. 1998; Siris et al. 2001). One overview of studies that attempted to predict osteoporosis-linked fractures with bone mineral density concluded: “Measurements of bone mineral density can predict fracture risk but cannot identify individuals who will have a fracture. We do not recommend a programme of screening menopausal women for osteoporosis by measuring bone density” (Marshall, Johnell, and Wedell 1996, 1254). See also Nelson et al. 2002.

²¹ For a history of the concept of osteoporosis, see Klinge 1998.

use of the density measure, which, he argues, “affects the way we conceptualize the skeleton (or fail to), and the way we direct (or misdirect) our research,” and “blind[s] us to the biology of bone” (510).

Weaving together these threads—increasing lifetime risk, new disease definitions, and easier measurement—produces an epistemological transformation in our scientific accounts of bones and why they break. The transformation is driven by a combination of cultural forces (why are fracture rates increasing?) and new technologies generated by drug companies interested in creating new markets, disseminated with the help of market forces drummed up by the self-same drug companies, and aided by consumer health movements, including feminist health organizations such as the Society for Women’s Research, which argue that gender-based differences in disease have been too long neglected.

Analyzing bone development within the framework of sex versus gender (nature vs. nurture) makes it difficult to understand bone health in men as well as women. Those trying to decide on a proper standard to measure fracture risk in men (should they use a separate male baseline or the only one available, which is for young, white women?) struggle with this problem of gender standardization (Melton et al. 1998). There are differences between men and women, although osteoporosis in men is vastly understudied. In a bibliography of 2,449 citations of papers from 1995 to 1999 (Glock, Shanahan, and McGowan 2000), only 47 (2 percent) addressed osteoporosis in men. But making sense of patterns of bone health for either or both sexes requires a dynamic systems approach. A basic starting place is to ask the development question.

For instance, we find no difference in bone mineral density in (Caucasian) boys and girls under age sixteen but a higher bone mineral density in males than in females thereafter (Zanchetta et al. 1995). This difference (combined with others that develop during middle adulthood) becomes important later in life, since men and women appear to lose bone at the same rate once they have reached a peak bone mass; those starting the loss phase of the life cycle with more bone in place will be less likely to develop highly breakable bones. Researchers offer different explanations for this divergence. Some note that boys continue to grow for an average of two years longer than girls (Seeman 1997). The extra growth period strengthens their bones by adding overall size. Others point additionally to hormones, diet, physical activity, and body weight as contributing to the emerging sex (or is it gender?) difference at puberty (Rizzoli and Bonjour 1999).

So differences in bone mineral density between boys and girls emerge during and after puberty, while for both men and women peak bone mass

and strength is reached at twenty-five to thirty years of age (Seeman 1999). Vertebral height is the same in men and women, but vertebral width is greater in men. The volume of the inner latticework does not differ in men and women, but the outer layer of bone (periosteum) is thicker in men. Both width and outer thickness strengthen the bone. In general, sex/gender bone differences at peak are in size rather than density (Bilzikian, Kurkland, and Rosen 1999).

This life-cycle analysis reveals three major differences in the pattern of bone growth and loss in men compared with that in women. First, at peak, men have 20 to 30 percent more bone mass and strength than women. Second, following peak, men but not women compensate for bone loss with new increases in vertebral width that continue to strengthen the vertebrae. Over time both men and women lose 70 to 80 percent of bone strength (Mosekilde 2000), but the pattern of loss differs. In men the decline is gradual, barring secondary causes.²² In women it is gradual until perimenopause, accelerates for several years during and after the menopause, and then resumes a gradual decline.²³ Lis Moskilde (2000) points out that the rush to link menopause to osteoporosis has led to the neglect of two of the three major differences in the pattern of bone growth between men and women. Yet these two factors are specifically linked to physical activity, and thus amenable to change earlier in life.

Indeed, many studies on children and adolescents address the contribution sociocultural components of bone development make to male-female differences that emerge just after puberty (see table 1). But the overwhelming focus on menopause as the period of the life cycle in which women enter the danger zone steers us away from examining how earlier sociocultural events shape our bones (see Lock 1998). Once menopause enters the picture, the idea that hormones are at the heart of the problem overwhelms other modes of thought.²⁴ Nor is it clear how hormones affect

²² A secondary cause might be bone loss due to an eating disorder or a metabolic disease, or the prolonged use of a bone-leaching drug such as cortisone.

²³ When I use the words *men* and *women* I refer to particular populations on which these studies were done. These are mostly Caucasian and Northern European or North American. Most of the studies have been done since the 1980s, but bone size, shape, and growth patterns would have differed at the beginning of the twentieth century compared with their appearance at the beginning of the twenty-first. I will not make these points every time I use these words.

²⁴ So powerful is the focus on old age that the long NIH bibliography on menopause completely ignores the possible importance of pregnancy and lactation on bone development. These two processes are profoundly implicated in calcium metabolism, and if there is *no* effect on later bone strength it would be important to find out why. What physiological

bone development and loss. In childhood, growth hormone is essential for long bone growth, the gonadal steroids are important for the cessation of bone growth at puberty, and probably both estrogen and testosterone are important for bone health maintenance (Damien, Price, and Lanyon 1998). The details at the cellular level have yet to be understood (Gasparino 1995).

Basic bone biology

In the fetus, cartilage creates the scaffolding onto which bone cells climb before secreting the calcium-containing bone matrix that becomes the hard bone.²⁵ The cells that secrete the bone matrix are called osteoblasts. As they grow, bones are shaped by the strains and stresses put on them by the activity of their owner. Osteoblasts deposit matrix at some sites, while another cell type, the osteoclast, can chip away at areas of too much growth. Growing bones change shape through this give and take of osteoblast and osteoclast activity in a process called bone remodeling.²⁶ Long bones increase in length throughout childhood by adding on new material at their growing ends. These growth sites close as a result of hormonal changes during puberty, but bone reshaping continues over the course of a life (Currey 2002).

Bone contains two important types of tissue, which can be seen (fig. 1, A) if one cuts it across the middle. The outer dense, hard layer is called compact tissue; the inner layer contains cancellous tissue consisting of a latticework of slender fibers. The fibers of this interior bone lattice fuse into longer structures called trabeculae (Latin for “small beam”) that crisscross the interior of the bone. The periosteum (literally, “around the bone”), a layer of tissue through which blood vessels and nerves pass into the interior, covers the bone.

Osteoblasts clinging to the periosteum and around the trabecular struts of the bone’s interior can produce new bone in both locations. Osteoblasts can also transform into osteocytes, cells found in large numbers inside the hard bone tissues (Currey 2002). Osteocytes probably play an important

mechanisms protect the bone of pregnant and lactating women? This is an example of a biological question that lies fallow because of the focus on supposed estrogen deficiency in old age.

²⁵ The bone matrix is made up primarily of a substance called hydroxyapatite that is mostly composed of crystalline forms of the molecules calcium phosphate, calcium carbonate, and small amounts of magnesium, fluoride, and sulfate.

²⁶ One memory device for remembering which cell is which is to think that osteoBlasts Build bone and osteoClasts Chomp on bone.

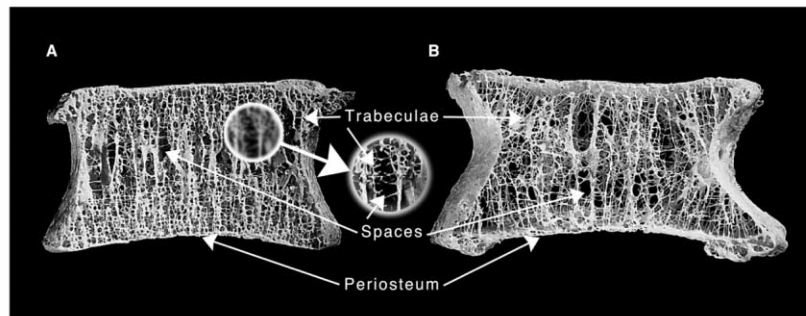


Figure 1 Vertebral structure. Scanning electron micrographs of longitudinal sections of human vertebrae. This image is a modification of one published in Mosekilde 2000. (A) Healthy vertebra showing the trabecular structure of the cancellous bone (inset) and the surrounding periosteum. Note the regular vertical arrangement and density of the trabeculae. (B) A vertebra exhibiting osteoporosis. Note the increased number and size of spaces where cross struts have broken, as well as the less organized and less dense trabecular structure.

role in bone regeneration when they produce chemical signals that tell osteoblasts that the bone is under mechanical strain and needs to grow (Mosley 2000). Osteoblasts cannot form new bone unless the surface on which they sit is under a mechanical strain, which explains why exercise remains such an important component of bone health while weightlessness in space or prolonged bed rest result in the loss of bone thickness.²⁷ Moreover, osteoblasts only add new bone on preexisting surfaces. A person with osteoporosis develops breaks in the tiny cross beams, and these widen into holes that riddle the bone's interior (fig. 1, B). A lost strut cannot be replaced because there is no old surface on which to lay down a new mineral layer. A thinning strut, however, can thicken again if the osteoblast produces more new bone than the osteoclast breaks down (Parfitt 1988; Mosekilde 2000).

Bone development, then, is profoundly influenced by what physiologists call functional adaptation. Although a great deal remains to be understood about the biology of use and disuse, some basic principles are already evident. First, both disuse and predictable moderate use result in bone resorption and increased porosity. However, dynamic strain, that is, strain that is unpredictable and of varied impact level, can lead to a linear increase in bone mass (Mosley 2000).²⁸ Bones may adopt strain thresholds such

²⁷ Stress can be from direct impact or from tension placed on the bones by attached muscles. For more details on the importance of mechanical strain on bone development, see Skerry and Lanyon 1995; Mosekilde 2000; Mosley 2000.

²⁸ In animal models it is possible to induce new bone formation (modeling) without first having caused bone resorption (Pead, Skerry, and Lanyon 1988).

that only strains above such thresholds induce new bone formation. Strain thresholds may change over the life cycle. Perhaps the decline in estrogen associated with menopause resets the threshold to a higher strain level, thus requiring very high levels of bone stress to stimulate new bone formation. Such dynamic theories allow us to understand how behavior (e.g., changing forms of exercise) and hormonal changes in the body might together produce bone loss or gain (Frost 1986, 1992).

Even such a simplified account of bone development and maintenance shows how hard it can be to understand why people in one group break their bones more often than people in another. Groups may differ in peak bone size even if bone loss later in life is the same. The trabeculae on the bone's inside might be thicker in one group than another, or the outside, compact bone layer might be thicker. There could be less bone loss or a reduction in bone turnover (the balance between osteoclast and osteoblast activity). Trabecular loss could result from thinning rather than perforation, or there could be more new bone formation in the periosteum or less resorption in the bone's interior. What is most striking about the medical literature on osteoporosis is that "whether these differences in bone size, mass, or structure, or bone turnover among ethnic groups or between men and women even partly account for the corresponding group differences in fracture rates is unknown" (Seeman 1997, 517).

Genes, of course, are involved in all of the events described in the previous few paragraphs. Rather than as causes of bone construction and destruction, however, genes are best understood as mediators, suspended in a network of signals (including their own) that induce them to synthesize new molecules.²⁹ The molecules they make may help to produce more bone or to break down existing bone. Either action may, in turn, be a direct effect (e.g., making a structural element such as collagen) or an indirect effect (e.g., causing the death or sustaining the life of bone-making cells). Researchers have identified over thirty genes that affect bone development either positively or negatively in mice (Peacock et al. 2002), and scientists continue to identify genetic variants affecting bone density in humans (Boyden et al. 2002; Little et al. 2002; Ishida et al. 2003).

Finally, how do hormones fit into all of this? Part of the initial logic of thinking about osteoporosis as a basic biological (sex) difference be-

²⁹ One review states that mechanical receptors transform signals from deforming bones into changes in the shape of DNA regions that regulate the activities of genes involved in bone formation. The authors write that "bending bone ultimately bends genes" (Pavalko et al. 2003, 104).

tween men and women derives from the observation that bone thinning increases dramatically around the time of menopause. Most thus assume that declining estrogen causes bone loss. Since estrogen codes in most people's minds as a quintessentially female molecule, it becomes extraordinarily difficult to conceptualize osteoporosis as a disease with many contributors stretching over the entire life cycle. Here, gender constructs (Fausto-Sterling 2000) combined with the profits derived from selling estrogen replacement have contributed mightily to shaping the course of scientific research in this field. Estrogen, though, is only one of a number of hormones linked to bone physiology.

At least three major hormone systems acting both independently of one another and through mutual influence regulate bone formation and loss. Fascinatingly, at least two of these operate at times through the brain and the sympathetic (involuntary) nervous system.³⁰ The first system includes three major hormones that maintain proper calcium levels throughout the body, dipping into the bone calcium reservoir as needed.³¹ The hormones (the active form of vitamin D; parathyroid hormone [PTH], which is made by a small pair of glands called the parathyroid glands; and calcitonin, which is secreted by the thyroid glands) regulate blood calcium levels and bone metabolism.³² At low concentrations PTH maintains a stable level of mineral turnover in the bone, but at high levels it stimulates osteoclast activity, thus releasing calcium into the bloodstream.³³ Although calcitonin counteracts the effects of PTH on osteoclasts, its functions and mode of action are still poorly understood, but PTH affects bone, kidney, and intestine using vitamin D as an intermediary—a point that returns us to the contributions of sunlight and diet. Our diets and cellular machinery provide inactive forms of vitamin D, but these require the direct energy from sunlight hitting the skin to change into potentially active forms. Final transformations from inactive to active forms of vitamin D occur in the liver and kidney (Bezkorovainy and Rafelson 1996).

Although gonadal hormones—both estrogens and androgens—are

³⁰ Physiological functions such as heart and breathing rate and energy metabolism are regulated through involuntary nerves belonging to the sympathetic and parasympathetic nervous systems. These systems balance each other out by stimulating or inhibiting various functions. They are controlled through brain centers without our having to think about them.

³¹ All cells, but especially nerve and muscle cells, need calcium. So bone is essential not only for structural support but also to maintain healthy calcium levels throughout the body.

³² The active form of vitamin D is 1,25-dihydroxycholecalciferol.

³³ Parathyroid hormone also increases Ca^{++} reabsorption in the kidney and absorption in the small intestine.

clearly important for bone development and maintenance, how they regulate bone metabolism remains uncertain (Kousteni et al. 2001, 2002). Recently, some fascinating studies done on mice have suggested that both androgens and estrogens operate in a fashion unusual for steroid hormones—by preventing the death of bone-forming cells without stimulating new gene activity. Whether these results will hold for humans remains to be seen.³⁴ Other information from animal models suggests that bone response to mechanical strain requires the presence of an estrogen receptor on the osteoblast cell surface (Lee et al. 2003), but a clear story of the role of estrogens and androgens in bone formation and maintenance throughout the life cycle remains to be told.

Last but certainly not least a hormone called leptin, announced to the world with great fanfare in 1995 as a possible “magic bullet” for weight control (Roush 1995), also affects bone formation. Like the sex steroids, leptin works via a relay system in the hypothalamus, a part of the brain linked to the pituitary gland. Fat tissue produces leptin, which signals specialized nerve cells in the hypothalamus; these activated neurons produce two effects—lowering the appetite and stimulating basal metabolism (via the sympathetic nervous system). In mice, leptin has a second, apparently independent effect, also mediated through the hypothalamus and the sympathetic nervous system. Increased leptin signals nerves in the bone to depress bone formation. This presents an interpretive paradox: obesity provides some protection against osteoporosis. But the more fat cells, the more leptin is made, which in theory ought to depress bone formation. There are several possible explanations for this paradox. In mice it may be that the very overweight body becomes insensitive to its high leptin levels, just as obesity contributes to insulin insensitivity in type 2 diabetes. Or the stimulation of bone formation from the mechanical stress of increased weight might trump the effects of leptin, and/or leptin physiology in mice and humans might differ in important ways.³⁵

In the next decade we will surely learn a lot more about the relationships among bone formation, leptin, and the sympathetic nervous system.³⁶ But we also must learn how to study the balances and interactions among all

³⁴ The negative effects of estrogen treatment come from the hormone’s more common mode of action—stimulating gene activities after binding to the nucleus. The researchers cited have a compound that has none of the gene-activity-stimulating actions but does behave like androgens and estrogens by preventing the death of osteoblasts. See also Moggs et al. 2003.

³⁵ Ducey et al. 2000; Flier 2002; Takeda et al. 2002; Harada and Rodan 2003.

³⁶ Leptin may also regulate the onset of puberty, thus linking gonadal hormones and the leptin hormone system (Chehab et al. 1997).

of the various factors that impinge on bone formation. How do social systems that influence what we eat, how and when we exercise, whether we drink or smoke, what kinds of diseases we get and how they are treated, and how we age, to name some most relevant to bone formation, produce a particular bone structure in a particular individual with a particular life history? To even begin to set up this problem in a manner that can stimulate future work and ultimately bring us better answers, we need to learn how to handle complex, dynamic systems. And so, finally, I turn to a discussion of two overlapping sets of ideas—developmental and dynamic systems theory.

Thinking systematically about bone

There are better ways to think about gender and the bare bones of sex. One cannot easily separate bone biology from the experiences of individuals growing, living, and dying in particular cultures and historical periods and under different regimens of social gender.³⁷ But how can we integrate the varied information presented in this essay in a manner that helps us ask better research and public policy questions and that, in posing better questions, allows us to find better answers? By *better*, I mean several things: in terms of the science I want to take more of the “curious facts” about bone into account when responding to public health problems. I favor emphasizing lifelong healthful habits that might prevent or lessen the severity of bone problems in late life, but I would also like us to have a better idea of how to help people whose bones are already thin. What dietary changes, what regimens of exercise and sun exposure, what body mass index work best with which medications? How do the medications we choose work? What unintended effects do they have? Finally, *better* includes an ability to predict outcomes for individuals, based on their particular life histories and genetic makeups, rather than merely making probability statements about large and diverse categories of people.

How can we get there from here? Below, I outline in fairly general form the possibilities of dynamic systems and developmental systems approaches. Such formulations allow us to work with the idea that we are always 100 percent nature and 100 percent nurture. I further point to

³⁷ I found one eloquent but wordless example on the Web in an article on causes of vitamin D deficiency. The short segment titled “Insufficient Exposure to Sunlight” was accompanied by a photograph of two women, standing in the blazing sun, covered from head to toe in burkas, clearly insufficiently exposed to sunlight but not for want of being outdoors in the sun.

important theoretical and empirical work currently under way by social scientists who study chronic diseases using a life-course approach. Before turning to the specifics of bone development, let me offer a general introduction to these complementary modes of thought.

Figure 2 presents a visual scheme of the larger systems arena. Ludwig von Bertalanffy is usually cited as the originator of “general systems theory,” a program for studying complex systems such as organisms as whole entities rather than the traditional approach of reducing the whole to its component parts (Bertalanffy 1969), but the idea of studying developmental outcomes as a result of the combined action of genes and environment began in the early twentieth century before a clear theoretical statement was achieved in the 1940s.³⁸

Systems theorists also write about the brain and behavior. D. O. Hebb (1949) linked psychology and physiology by thinking about how functional cellular groups develop in the brain, thus developing a form of systems theory called connectionism. As Esther Thelen and Linda Smith put it, “the connection weights between layers—the response of the network to a particular input—thus depend on the statistical regularities in the network’s *history* of experiences” (Thelen and Smith 1998, 580). Thus an organism’s current and future behaviors are shaped by past experiences via a direct effect on the strength of connections between cells in the brain.³⁹

The varied systems approaches to understanding development share certain features in common. All understand that cells, nervous systems, and whole organisms develop through a process of self-organization rather than according to a preformed set of instructions.⁴⁰ The varying rela-

³⁸ Brief histories of these ideas as well as accounts of present-day embryology, genetics, and evolution based on systems theory may be found in Waddington 1957; Kauffman 1993; Webster and Goodwin 1996; Schlichting and Pigliucci 1998; van der Weele 1999; Oyama 2000a, 2000b.

³⁹ The implications of these ideas for an integrative theory of the development of gender differences in behavior and psychological skills has not escaped me and is the subject of a work in progress. The explosion of knowledge about the plastic nature of brain development and an increasing understanding of neuroplasticity in adults suggests that far from being destiny, anatomy is dynamic history. A rich literature that joins mathematical models of nonlinear equations (Kelso 1995) has begun to join forces with experimental scientists who study animal behavior (Gottlieb 1997) and those who now use dynamic systems approaches to reconceptualize human behavioral development (Smith and Thelen 1993; Thelen and Smith 1994, 1998; Thelen 1995; Thelen et al. 2001).

⁴⁰ Among biologists the idea that genes provide such instructions is giving way to a systems account of cell function. The metaphor of the genome (DNA) as a blueprint or set of directions for building cells and organisms is giving way to a new metaphor—genomes

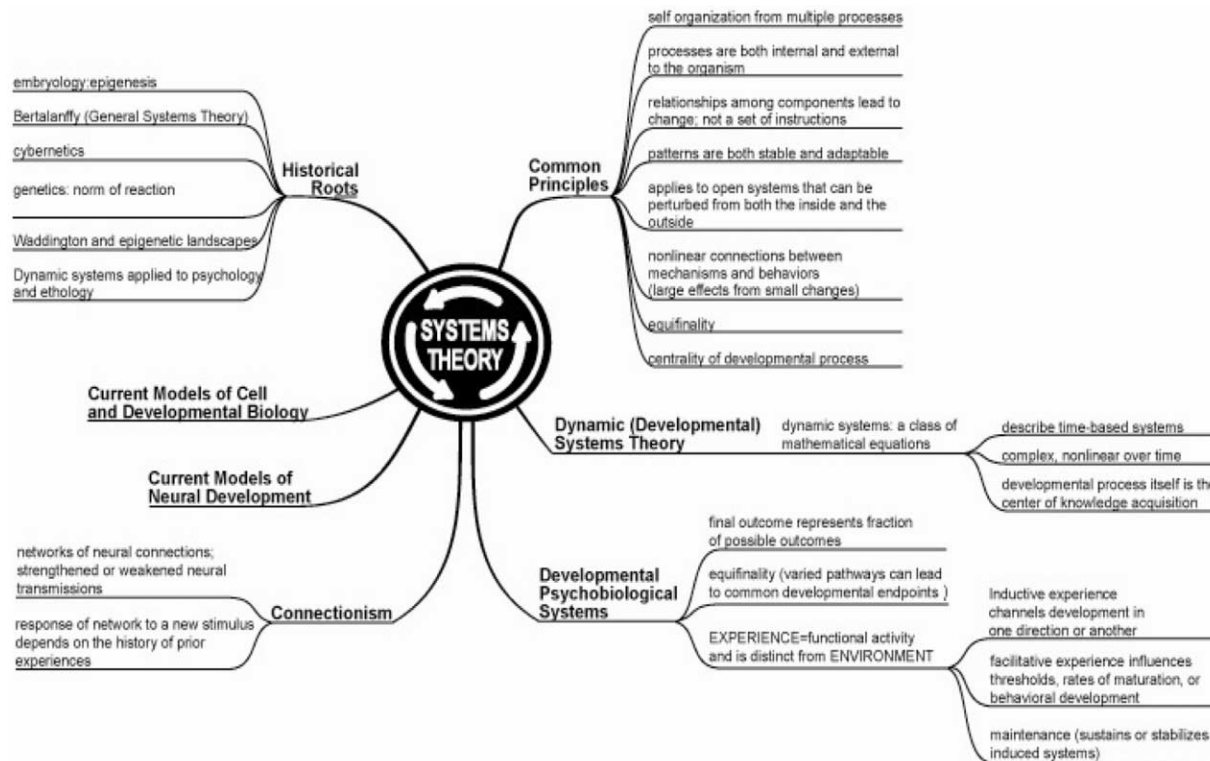


Figure 2 Overview of systems theories

tionships among system components lead to change, and new patterns are dynamically stable because the characteristics of the system confer stability. But if the system is sufficiently perturbed, instability ensues and significant fluctuations occur until a new pattern, again dynamically stable, emerges. Bone densities, for example, are often dynamically stable in mid-life but destabilize during old age; most medical interventions aim to restabilize the dynamic system that maintains bone density. But we really do not understand how the transition from a stable to an unstable system of bone maintenance occurs.

To address the bare bones of sex, I highlight, in figure 3, seven systems that contribute to bone strength throughout the life cycle.⁴¹ I also describe some of the known interrelationships between them.⁴² Each of the seven—physical activity, diet, drugs, bone formation in fetal development, hormones, bone cell metabolism, and biomechanical effects on bone formation—can be analyzed as a complex system in its own right. Bone strength emerges from the interrelated actions of each (and all) of these systems as they act throughout the life cycle. As a first step toward envisioning bone from a systems viewpoint we can construct a theoretical diagram of their interactions. The diagram in systems approaches can be thought of as a theoretical model, to be tested in part or whole and

as parts list (Vukmirovic and Tilghmann 2000; Tyson, Csikasz-Nagy, and Novak 2002). If the genome lists only the component parts (codes for RNA and protein), the location of the assembly directions becomes uncertain: one needs to specify a cell or organism's past history and current conditions in order to predict a current developmental event accurately. Cell biologists have now turned in earnest to complexity and systems theory to help learn the rules by which organisms are assembled. (See entire December 2002 issue of *Bioessays* devoted to "Modeling Complex Biological Systems.") In another example, authors extend and twist the book metaphor: "Just as words must be assembled into sentences, paragraphs, chapters and books to make sense, vital cellular functions are performed by structured ensembles of proteins . . . not by freely diffusing and occasionally colliding proteins" (Sali et al. 2003, 216).

⁴¹ I use Peter Taylor's definition of systems as "units that have clearly defined boundaries, coherent internal dynamics, and simply mediated relations with their external context" (personal communication 2003).

⁴² This choice of systems emerges from the data presented earlier in this article. Since this is a model, others might argue for dividing the pie in a different way. To keep the diagram readable and the discussion manageable, I have not emphasized that the entire grouping of systems is embedded in a larger system I call "general health." There are many disease states that secondarily affect bone (e.g., kidney disease or endocrine disorders) by affecting calcium metabolism or preventing exercise. The relationships among the systems affecting bone strength would be shifted in dramatic ways worthy of study in their own right under such circumstances.

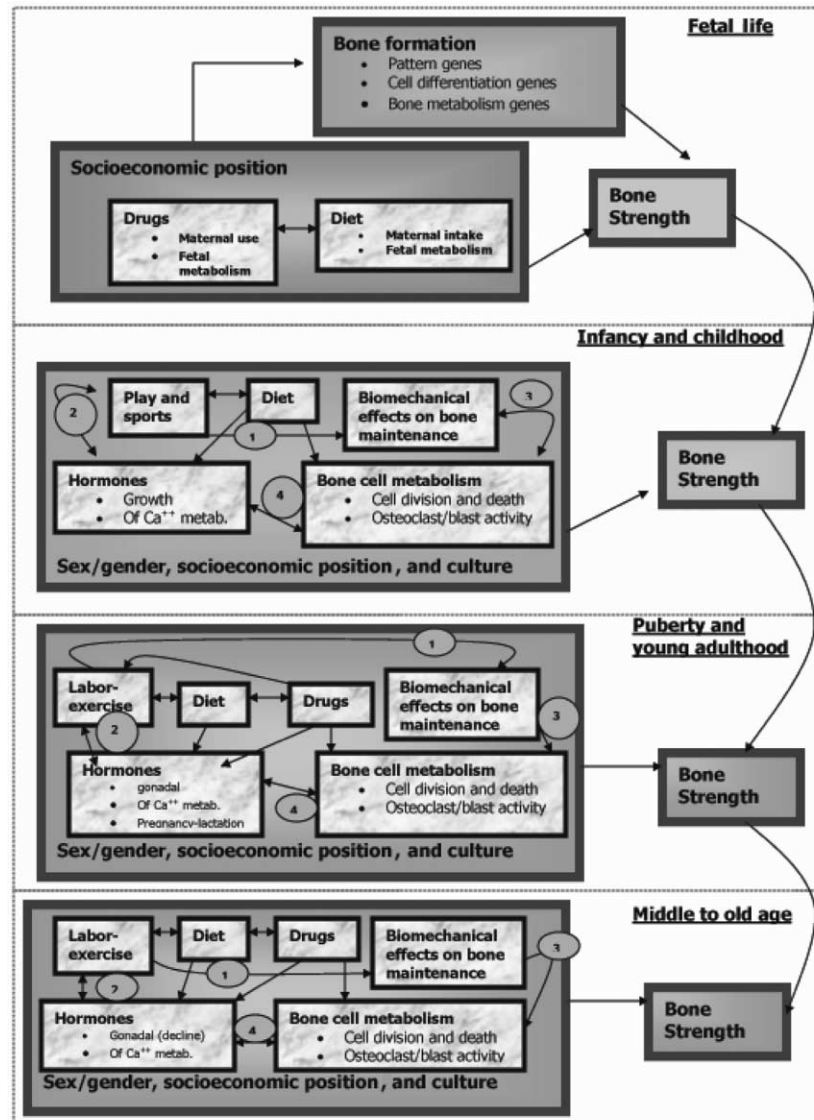


Figure 3 A life history-systems overview of bone development. (1) Physical activity has direct effects on bone cell receptors and indirect effects by building stronger muscles, which exert physical strain on bones, thus stimulating bone synthesis. (2) Physical activity that takes place outdoors involves exposure to sunlight, thus stimulating vitamin D synthesis, part of the hormonal system regulating calcium metabolism. (3) Biomechanical strain affects bone cell metabolism by activating genes concerned with bone cell division and bone (re)modeling. (4) Hormones affect bone cell metabolism by activating genes concerned with bone cell division, cell death, bone (re)modeling, and new hormone synthesis.

modified as needed.⁴³ As ways to describe each component system using numerical proxies become available, the pictorial model can provide the framework for a mathematical model. Figure 3 represents one possible diagram of a life-course systems account of bone development.

This feminist systems account embeds the proposed subsystems within the dimensions of gender, socioeconomic position, and culture.⁴⁴ Consider the diet system. Generally, of course, diet is shaped by culture and sub-culture, including race and ethnicity (Bryant, Cadogan, and Weaver 1999). But gender further influences diet. For example, one study reports that 27 percent of U.S. teenage girls (compared with 10 percent of adolescent boys) who think they weigh the correct amount are nevertheless trying to lose weight (Walsh and Devlin 1998). It may also be true that there are sex/gender differences in basal metabolism rates that influence food intake.

Figure 3 also indicates the cumulative effects of diet on bone formation. Key events may be clustered at certain points in the life cycle.⁴⁵ For example, adolescent girls in the United States often diet more and exercise less than during earlier childhood. Diseases such as anorexia nervosa, which have devastating effects on bone development, may also emerge during adolescence. As Yoav Ben-Shlomo and Diana Kuh (2002) point out, such clustering of adverse events is common and may be thought of in terms of “chains of risk” (or benefit). In a life-course approach, prior events set the limits on later ones. If girls and women enter into adulthood with weakened bones, therefore, they can rebuild them, but their peak density may be less than if they had built stronger bones in adolescence.⁴⁶ Alternatively, achieving a safe peak bone density might require more sustained and intense work for a person of one history compared with a person of a different history.

Sex/gender, race, class, and culture also differentiate individuals by forms of play in childhood and beyond (Boot et al. 1997), by choices of formal exercise programs, and, in adulthood, by forms of labor, physical and otherwise. In analyzing the system of physical activity one again applies life-course principles by considering that what happens at any one point

⁴³ Choice of model has profound implications. For a discussion of a lifestyle model of disease that emphasizes individual choice vs. a “social production model,” see Krieger and Zierler 1995. For an update on current theories of social epidemiology, see Krieger 2001.

⁴⁴ To the extent that race is a legitimate category separate from class and culture, I will incorporate it into the bone systems story in pt. 2 of this work. For a model of social pathways in childhood that lead to adult health, see Kuh and Ben-Shlomo 1997.

⁴⁵ Bonjour et al. 1997; Boot et al. 1997; Perry 1997; Wang et al. 2003.

⁴⁶ For the effects of dietary calcium later in life, see Heaney 2000.

builds on what has gone before. Important events with regard to bone development may be clustered and interrelated. For both the diet and physical activity systems, it should be possible to design mathematical models based on some measure of bone strength that would incorporate the effects of each of these social systems on bone development throughout the life cycle; once we have plausible models of each system, we can ask questions about their interactions.

The remaining four systems are often considered within the realm of biology, as if biology were separate from culture, although recent work from some medical epidemiologists challenges this distinction (Ellison 1996; Hertzman 1999; Lamont et al. 2000). The system of biomechanical effects on bone synthesis, for example, requires further investigation of all of its inputs (physical strain, activation of genes that stimulate bone cell development or death, etc. [Harada and Rodan 2003]), but these must then be studied in relationship to the gender-differentiated physical activity system. The different body shapes of adult men and women (related to hormones at puberty among other things) may also affect bone biomechanics, and we need, too, to know more about how growth and development affect the number of bone mechanoreceptors—molecules that translate mechanical stress in biochemical activity (Boman et al. 1998; Pavalko et al. 2003).

The impact of hormones on bone development and maintenance requires research attention of a sort currently lacking in the bone literature. We need to know both about the molecular biology of hormones and bone cell hormone receptors and about life-course effects on hormone systems (Ellison 1996; Worthman 2002). Finally, genes involved in bone cell metabolism, pattern formation, hormone metabolism, drug processing, and many other processes contribute importantly to the development of bone strength (Zelzer and Olsen 2003). Understanding how they function within both the local and global (body and sociocultural) networks contributing to bone development requires a systems-level analysis not yet found in the literature.

Conclusion

This article is a call to arms. The sex-gender or nature-nurture accounts of difference fail to appreciate the degree to which culture is a partner in producing body systems commonly referred to as biology—something apart from the social. I introduce an alternative—a life-course systems approach to the analysis of sex/gender. Figure 3 is a research proposal for multiple programs of investigation in several disciplines. We need to

ask old questions in new ways so that we can think systematically about the interweaving of bodies and culture. We will not lay bare the bones of sex, but we will come to understand, instead, that our skeletons are part of a life process. If process rather than stasis becomes our intellectual goal, we will improve medical practice and have a more satisfying account of gender and sex as, to paraphrase the phenomenologists, being-in-the-world.

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