AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY 70:145–160 (1986)

Poor Growth Prior to Early Childhood: Decreased Health and Life-Span in the Adult

GEORGE A. CLARK, NICHOLAS R. HALL, GEORGE J. ARMELAGOS, GARY A. BORKAN, MANOHAR M. PANJABI, AND F. TODD WETZEL
Normative Aging Study, VAOPC, 17 Court St., Boston, Massachusetts 02108 (G.A.C., G.A.B.), Biomechanics Laboratory, Section of Orthopedic Surgery, Yale University School of Medicine, New Haven, Connecticut 06510 (G.A.C., M.M.P., F.T.W.), School of Public Health, Boston University School of Medicine, Boston, Massachusetts 02118 (G.A.C.), Department of Biochemistry, George Washington University School of Medicine, Washington, D.C. 20037 (N.R.H.), and Department of Anthropology, University of Massachusetts, Amherst, Massachusetts (G.J.A.)

KEY WORDS Early growth, Vertebral neural canals, Adult health and life-span

ABSTRACT Previous studies in animal populations have shown that stunted neural and thymolymphatic growth early in development may result in permanently impaired neural and immune function, decreased body growth, vertebral wedging, and decreased life-span. In the human adult, small vertebral neural canal (VNC) diameters may reflect early stunted neural and immune development and impaired function that leads to decreased health (inferred by greater vertebral wedging) and life-span in the adult. VNC, which complete their growth by early childhood (age 4), are markers of early development in adults. On the other hand, features following general body growth, such as height, weight (represented here by vertebral body height) continues to grow until young adulthood. They are less reliable, because they readily experience catch-up growth (even in chronically stressed populations) and, unlike VNC, may mask poor early growth. To test associations between early growth and adult health and life-span in humans, we measured 2,060 VNC, vertebral heights, vertebral wedging, nerve-root tunnel lengths, severity of vertebral osteophytosis, and ages at death in 90 adult (aged 15–55 years) prehistoric skeletons (950–1300 A.D.). Tibial lengths were also measured in a subsample (n = 30). Multivariate, bivariate, and nonparametric analyses showed that small VNC are significantly associated with greater vertebral wedging and decreased life-span ($P < 0.05$–0.00001). VNC are independent of vertebral body heights and tibial lengths (general body growth). VNC, but not statural components, are useful in predicting adult health, presumably because they reflect neural and immune development and do not readily experience catch-up growth. Thus, longitudinal retrospective measures of early growth and adult health were systematically linked within individuals regardless of confounding factors operating over the 350-year time period. Since this research was completed, this model has repeatedly been independently confirmed in four living urban industrial populations. Longitudinal retrospective analysis was employed together with direct measures of VNC, neural and immune function. Together these results suggested that it may be essential to improve growth prior to early childhood in order to maximize adult health and life-span.

Received June 20, 1985; revision accepted August 13, 1985.

Previous studies examining relationships between early growth, adult health, and life-span have been ambiguous. For example, studies using nonhuman models have shown that early stunted growth results in better adult health and increased life-span (Lamb, 1977). Conversely, studies in human (e.g., Stoch and Smythe, 1976; Guagliardo, 1982) and animal (e.g., Pierpaoli, 1981) populations have also shown that poor early growth is associated with decreased adult health and life-span. We suggest these latter studies, that use anthropometric (morphometric) measures reliably reflecting neural and thymolymphatic growth curves, such as vertebral neural canals (VNC), head circumference, or tooth size, rather than those that following the general growth, such as weight and height, have so far been unambiguous in their results. They have consistently shown that poor early growth predicts decreased adult health and life-span.

The purpose of this article is to present a theoretical model and results that suggest that events affecting human prenatal and early postnatal growth and development have far-reaching effects on later growth, health, and life-span. Specifically, we tested the hypothesis that stunted VNC size generally predicts greater vertebral wedging and decreased life-span in adults.

Before we continue some definitions are in order. Stunted size reflects reduced genetic growth potential due to environmental stress and not merely small size per se. Health is defined here as the capacity to resist disease and not merely the absence of disease(s). Vertebral wedging (posterior vertebral heights divided by the anterior) reflects decreased skeletal mass and presumably accelerated bone loss. Thus, vertebral wedging, and especially decreased life-span, defines decreased health status in the adult. Lastly, some may require a regression formula or flow diagram to refer to a scheme as a "model." However, less parochially, a model is a preliminary representation of something serving as the plan from which the final, usually larger, object is to be constructed. The following plan is our model, of why we expect stunted early growth (i.e., small VNC) to be related to poor adult health (i.e., vertebral wedging and decreased life-span).

Vertebral neural canals generally complete their growth by early childhood (age 4). Moreover, after maturation VNC are remarkably stable in size and shape regardless of aging or occupation (Porter et al., 1980). Thus, in the adult VNC are valuable as markers of earlier development. Figure 1 compares a vertebra from a 4-year-old to an adult's. It can be seen that VNC size in the young child is roughly the same as in the adult. After early childhood, vertebral growth occurs primarily in the vertebral body.

The rationale for the expected covariation between small VNC, greater vertebral wedging, and decreased life-span in the adult (i.e., poor early growth producing decreased adult health) can be partially illustrated in Figure 2. Vertebral neural canal size (VNC growth represented on Figure 2 by neuro-osseous growth) has the same growth curve as the thymolymphatic tissues. These complete most of their growth prenatally and cease growth prior to early childhood. Although Figure 2 illustrates continued lymphoid growth until adolescence, Figure 3 shows that the cortex, which is most central to immunocompetence (see below), actually completes its growth and begins to atrophy at birth. The cortex of the thymus and the lymphatic system really complete their func-

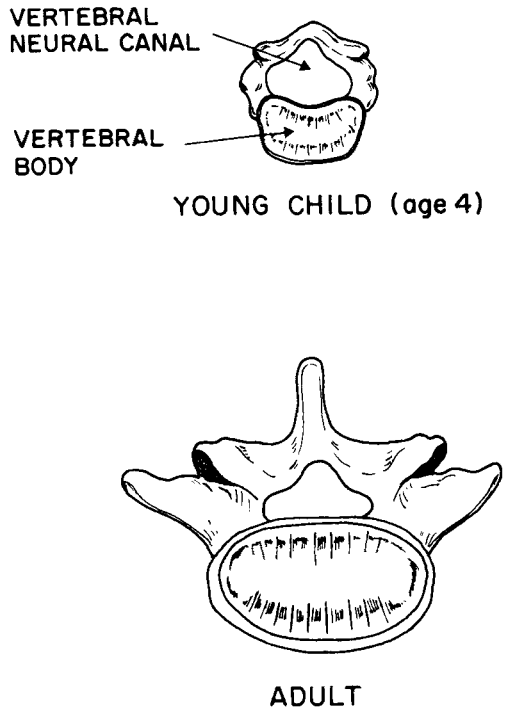

Fig. 1. Vertebra of young child in comparison with adult vertebra (cranial view).

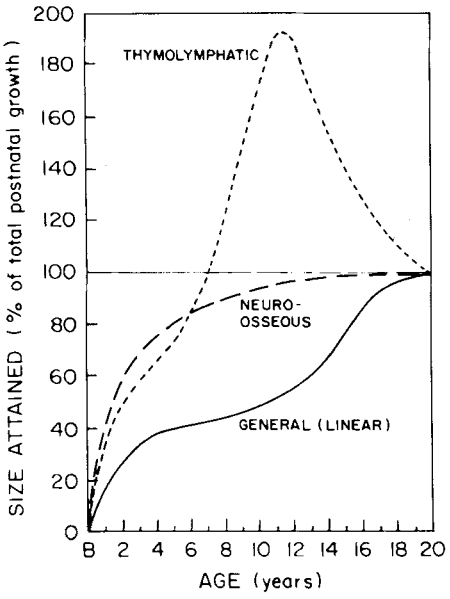

Fig. 2. Thymolymphatic, neuro-osseous, and general (linear) growth curves from birth to adulthood.

tional development before early childhood. Moreover, all these tissues should covary in development and stunting, because all of these tissues respond dramatically to many of the same anabolic and catabolic hormones, such as growth hormones and cortisol (Fabris, 1977; Cruess, 1982; Tannenbaum, 1984).

In humans, the thymic microenvironment is known to play a central role in the promotion of normal and aberrant T-cell maturation, especially in the cortex. Immature T cells migrate from the bone marrow to the cortex of the thymus, where they become functionally mature. Migration through a normal cortex, and interaction with indigenous thymocytes, are obligatory steps for the generation of competent T cells in the normal proportion of helper, effector, and killer T-cell ratios. After maturation in the cortex, lymphocytes migrate to the medulla of the thymus, and peripheral lymph organs (Haynes, 1984). Ironically, the cortex of the thymus, because of its fast developmental rate and early maturation, appears to be most vulnerable to prenatal and early post-

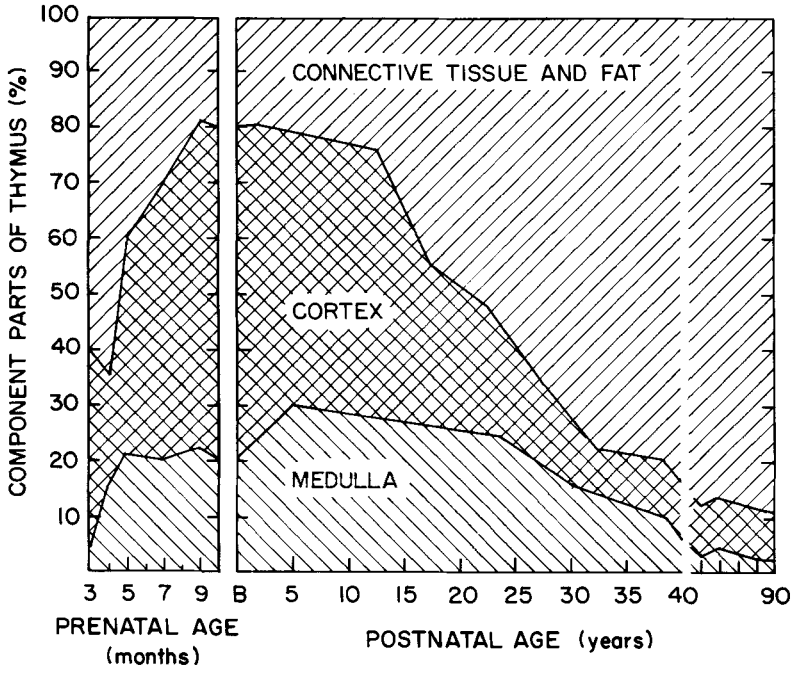

Fig. 3. Age-related changes in the human thymus (Boyd, 1936).

natal growth disruption, and its normal development is central to immunocompetence (Hammar, 1909, 1921; Boyd, 1936; Watts, 1969).

In the adult, when stunted VNC are seen, more dramatic stunted neural and immune development, with permanent dysfunction, should have also occurred. Skeletal development is known to be less susceptible to growth disruption than soft tissue, and among soft tissues the neural and thymolymphatic tissues appear to be most vulnerable to growth disruption during prenatal and early postnatal development. For example, studies in animal and human populations have found that prenatal and early postnatal stunted growth chiefly affect brain function and especially the thymus gland (e.g., Jose et al., 1973; Ford et al., 1976; Mugerwa, 1971; Gisler et al., 1971; Stoch and Smythe, 1976; Dubos et al., 1969; Sellmeyer et al., 1972; Winick, 1973). These tissues are most vulnerable, primarily because of their relatively fast growth rate and early period of maturation.

Among skeletal and dental tissue, neuro-osseous tissues, such as VNC, are most sensitive to growth disruption. For example, Platt and Stewart (1962) found that VNC sizes were several times more vulnerable to growth disruption (than these other skeletal and especially dental tissues). It is more commonly known, that small head circumference (HC) is a powerful indicator of poor growth through early childhood, and stunted HC reflects permanently impaired neurological function (Stoch and Smythe, 1963, 1976; Brandt, 1978). It is a complete myth that HC and brain (neural) growth is spared during systemic growth disruption during development. Neuro-osseous (HC or VNC) growth, compared to most features, is especially vulnerable to a wide variety of stressors that produce systemic growth disruption (Brook et al. 1984; Platt and Stewart, 1962).

If growth disruption outlasts the normal period of maturation of the particular feature, catch-up growth in size and physiological function cannot occur. This disruption may result in permanently stunted VNC, and permanently impaired neural and thymolymphatic growth and function (Pierpaoli and Sorkin, 1972; Dubos et al., 1969; Williams, 1981; Winick, 1969; Winick and Noble, 1966). Thus, if stunted VNC are observed in the adult, the individual should also exhibit permanent impaired neural and immune function, as a consequence of stunted development prior to early childhood.

Although it may seem that this model is theoretical, part of it has been repeatedly demonstrated in both human and animal populations. For example, prenatal and early postnatal growth disruptions resulting in permanently stunted thymic development and function in humans have been called "nutritional thymectomy" (Jose et al., 1973) and "autothymectomy" (Watts, 1969; see also Miller, 1978).

Such stunted thymic development produces similar biobehavioral changes in congenitally athymic mice and in mice whose immature thymus glands have been surgically removed. In mice, these changes include vertebral wedging and decreased life-span as well as accelerated loss of T cells, autoimmune diseases, disordered neuroendocrine function (especially in circadian rhythms of catecholamines and cortisol) and reduced life-span (Pierpaoli and Sorkin, 1972; McGillis et al., 1983). Histologically, these changes are remarkably similar to those seen in normal aging, and they have been called premature senescence, wasting syndromes, and accelerated aging (e.g., Zubriran and Gomez-Mont, 1953; Arnold et al., 1970; Hammar, 1921).

Ironically, Hammar's (1902; 1921) research, that suggested a poorly developed thymus (and lymph system which grows, matures, and atrophies at the same time as the thymus) was a potential major cause of illness in children (thymus lymphaticus). Thymus lymphaticus was rejected in the 1920's, because not all thymus (and lymph) glands were found to necessarily atrophy with age. Such dogma continues today. For example, in dismissing the accuracy (and utility) of Hammar's research (Kendall, 1981) notes that subsequent research consistently has shown that the thymus gland exhibits tremendous variability in thymic atrophy and function with age.

However, the whole point of our research, and others, is that the variability of growth, function, and atrophy in the thymus with age, is caused primarily by its sensitivity to growth disruption during its brief and rapid development. If growth disruption outlasts its normal period of development, or just one of its components, such as its cortical development, it results in permanently impaired growth and function for that particular feature. Moreover, our model extends to neuro-

osseous tissues as well as neural and thymolymphatic growth and function.

It has been suggested (Pierpaoli, 1981) that listing all the possible effects of early growth disruption is pointless, because the neural and immune systems are so inextricably linked during development. Consequently, we suggest that as anthropologists interested in fundamental and systemic causes of illness (rather than single isolated infectious diseases, such as HTLV III/LAV "causing" acquired immune deficiency) use the term stunted neural-immune development or more simply SNID. The term helps to categorize individuals with acquired neurological and immunological diseases due to poor early growth due to a wide variety of environmental stressors. Viruses and a variety of infectious diseases should be more frequent and more problematic in individuals with SNID. Using the term may focus attention on poor health status due to poor growth as a result of poor nutrition, poverty, etc., rather than a "cure" for a disease. Thus, we have presented a model that describes a central mechanism that details why VNC in the adult reflect poor growth prior to early childhood, and why poor early growth should result in poor adult health and decreased life-span.

MATERIAL AND METHODS

Population

We used the Dickson Mounds prehistoric (950–1300 A.D.) skeletal population, located in Illinois, to test our hypotheses. According to previous bioarcheological investigations these Amerindians changed their lifestyle (culture) from Pre-Mississippian (PreMiss.) hunting and gathering to Mississippian (Miss.) maize horticulture (Lallo, 1973). The extent of their reliance on maize and its impact on growth and health within and between cultures has been dealt with elsewhere (e.g., Clark, 1985; Clark et al., 1985; Goodman et al., 1984; Blakey and Armelagos, 1985; Harn, 1974, 1984). Our purposes here do not require a knowledge of what caused poor growth (small VNC). We are primarily interested in the relationship between poor early growth (not its source) evidenced by small VNC and adult health and life-span.

Advantages of archeological populations

Testing associations between early growth, adult health, and life-span in archeological skeletal populations is valuable for three reasons. First, longitudinal retrospective relationships between markers of early growth (VNC) and adult health and life-span can be computed instantly. This greatly reduces the time otherwise necessary to test such hypotheses between early growth and adult health within the same individual (even across 18 generations). Second, even though a natural experiment is used, a variety of confounding factors can still be controlled, such as sex, age, cultural affiliation, and other skeletal morphometrics. Third, using an archeological population permitted a conservative test of our hypotheses, because the environmental, social, and biological factors operating over a 350-year period presumably made it less probable that small VNC would be consistently found in the younger age-at-death groups or correlated with wedging. Moreover, the fact that small VNC are found exclusively in the younger age-at-death groups (<35 years) suggests that death was due to physiological stress that occurred early in development, leading to decreased adult life-span. Trauma was probably not the cause of death; otherwise, small VNC would be randomly associated with age-at-death groups.

Limitations

The limitation of using a prehistoric skeletal population is that direct measures of VNC, neural, and immunological growth and function are not possible. Thus, this is a preliminary investigation at least as far as causality is concerned.

Measurements

The skeletons (n = 90) were in excellent condition. All skeletons were screened to exclude pathological specimens such as those with neural arch defects, which might confound analysis. Following established methods, measurements were taken (by G.A.C.) from 1,073 thoracic and lumbar vertebrae. All continuous measures, except of tibiae, were recorded with vernier calipers to the nearest tenth of a millimeter.

These measurements include VNC (Fig. 4, top) in the anteroposterior (AP) and transverse (TR) diameters (n = 2,060) (Eisenstein, 1983), anterior and posterior vertebral body heights (VH) (Ericksen, 1976) (Fig. 4, bottom), wedging (posterior divided by anterior vertebral body heights) (Milne and Lauder, 1976), nerve root tunnel length (distance) (Panjabi et al., 1983), and vertebral osteophytosis (VO). VO was rated 1–4 for severity

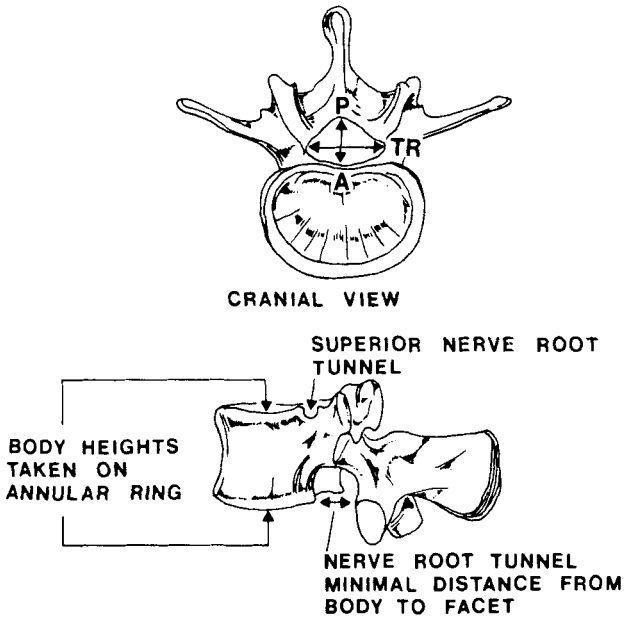

Fig. 4. AP and TR spinal (i.e., vertebral) canal diameters of nerve root tunnels.

(Nathan, 1962) on the inferior and superior margins of the vertebral body divided into quadrants (not in VNC or in nerve roots). The actual severity of VO was derived by adding the total severity for the segment. This permitted systemic rather than local (traumatic) VO to be considered. In a subsample (n = 30), minimum tibial lengths were measured by means of a standard osteometric board (Bass, 1971).

Age, sex, and cultural determination

Skeletal age at death, sex, and cultural affiliation were established by other investigators using bioarcheological techniques (see Lallo, 1973; Harn, 1984). These factors were not divulged prior to analysis so that measurement would not be biased.

We used 10-year age-at-death intervals: 15–25 (n = 18); 25–35 (n = 18); 35–45 (n = 21); 45–55 (n = 23). This reduced the miscalculation of age at death. Accuracy was above 90%. There were 41 male and 40 female skeletons: 13 male and 13 female PreMiss. skeletons; 26 male and 26 female Miss. skeletons. (Samples sizes depend on missing values.)

Statistical analysis

Statistical tests were performed by standardized multiple regressions, zero-order correlations, and two-tailed t tests for equal and unequal variances (SAS Institute, 1982). Sign tests were used to determine significant trends (Thomas, 1976).

We approached analysis in two ways. First we averaged each type of vertebral morphometric within the thoracic and the lumbar segments. This allowed particular morphometrics to be compared as segment morphometrics (L1–L5; T1–T12). The second tract examined the morphometrics at each vertebral level (L1, L2, etc.).

In order to insure that grouping the morphometrics into segments was valid, their internal consistency within the lumbar and thoracic segments was assessed by coefficient alpha (CA). A CA above 65% was recognized as sufficient to reduce the data set (SAS Institute, 1982). In the lumbar segment, all CAs were above 83% except for wedging, which was 65% (see Table 1). In the thoracic segment, the CAs (see Table 2) were above 90% except for vertebral osteophytosis (82%) and wedging, which was below 65%. Since thoracic wedging was below 65%, it was excluded from segment analysis.

The CA values for the VNC (>83%) were high, and this suggested that small VNC were stunted systemically and that the presence of small VNC was not an isolated phe-

TABLE 1. Internal consistency of lumbar region

Variable	Coefficient alpha
1. Spinal canal shape (Anteroposterior/ Transverse)	0.83
2. Anteroposterior spinal canal diameter	0.83
3. Transverse spinal canal diameter	0.85
4. Lumbar wedging (Post. body height/Ant. body height)	0.65
5. Posterior body height	0.92
6. Vertebral osteophytosis	0.86

TABLE 2. Internal consistency of thoracic region

Variable	Coefficient alpha
1. Spinal canal shape (Anteroposterior/ Transverse)	0.85
2. Anteroposterior spinal canal diameter	0.91
3. Transverse spinal canal diameter	0.90
4. Anterior body height	0.91
5. Posterior body height	0.94
6. Vertebral osteophytosis	0.82

nomenon within the vertebral column. Further analysis that suggests that small VNC were actually stunted in growth is detailed in the discussion section. Thus, except for thoracic wedging, all morphometrics were internally consistent and could be reliably grouped in thoracic or lumbar segments. Although wedging was present in the thoracic, it could not be reduced reliably into a segment value. This was probably due to the high number (12) of thoracic vertebrae, and the localized nature of vertebral wedging that occurs in the midthoracic region. The lumbar segment was reliable probably because it has fewer vertebrae (5) and carries more weight than the thoracic. It should more readily show the effects of compression and wedging. As a result, only the lumbar segment was used to test relationships between VNC and wedging.

For natural (realistic) experiments (with no artificial control over variables) strengths of correlations should be categorized as follows: 0.10 (slight); 0.20 (medium); 0.50 (large) (Cohen and Cohen, 1975).

RESULTS

Vertebral size and growth: Dickson vs. modern populations

Before we could begin analysis, it was important to determine whether Dickson vertebrae appeared similar in growth patterns and size to the vertebrae found in modern populations. For example, if VNC growth continues through early adulthood, individuals dying in the youngest age-at-death period would normally have smaller VNC than would survivors.

Although the need for longitudinal data is unquestioned, there does seem to be some validity for inferring heterochronic and kinetic growth patterns from static adult skeletal material. According to zero-order correlation and t tests, there was no significant VNC growth in the 15–25 age-at-death group for thoracic and lumbar AP and TR diameters. Interestingly, in modern populations thoracic vertebrae cease growth earliest and the lumbar latest, especially in the TR diameters (Hinck et al., 1966). This apparently was also the case in Dickson populations, as suggested by the analysis in the 15- to 25-year-olds (thoracic TR: $r = -0.08$, n.s., $n = 17$; AP: $r = 0.09$, n.s., $n = 17$; cf. lumbar TR: $r = -0.26$, n.s., $n = 18$; AP: $r = 0.10$, n.s., $n = 18$).

The ability to use adult skeletal material in inferring growth patterns between homochronic and heterochronic features is further suggested by analysis of the VNC diameters and tibial length. Lumbar TR but not AP diameters were correlated with tibial length (TR: $r = 0.52$, $P < 0.01$, $n = 27$; AP: $r = -0.17$, n.s., $n = 29$). Presumably this occurred because, unlike other VNC diameters, TR diameters grow somewhat after early childhood (about 3 mm or 20%) (Hinck et al., 1966), and they share more of the tibial growth curve than the AP diameters, which cease growth sooner. Similar results between TR and AP diameters and tibial lengths in adults have been found in adult skeletal material (Porter, 1985).

We checked growth of vertebral height (VH) in the 15- to 25-year-old age-at-death group because, unlike VNC, in modern populations VH (trunk growth) normally continues to grow into the midtwenties. Results for posterior VH in Dickson populations suggest that growth was continuing (thoracic: $r = 0.62$, $P < 0.01$, $n = 17$; lumbar: $r = 0.60$, $P < 0.01$, $n = 18$). Patterns for the anterior heights were equivalent. Thus, generally

adult skeletal material does appear to have some utility in assessing growth patterns. More important, Dickson vertebrae did appear to behave like those found in modern populations. VNC growth appeared to be completed by young adulthood and vertebral heights appeared to be continuing to grow.

Lumbar neural canal size and wedging

Our model suggested that there should be an inverse relationship between VNC size and wedging. Bivariate zero-order correlations and t tests, for combined age and sex groups, showed that individuals with smaller VNC TR diameters have greater vertebral wedging. This inverse correlation is moderate to large, linear, and highly significant ($r = -0.30$, $P < 0.01$, $n = 87$). The VNC AP diameters tend to show the same relationship, but they are neither as strong, nor as significant ($r = -0.19$, $P < 0.08$, $n = 87$). Similar bivariate analysis, for all age-at-death groups, showed similar inverse tendencies, and these inverse relationships became strongest in the oldest age-at-death group. For details see Clark (1985).

Table 3 shows four standardized multiple regression equations. The dependent variables were either TR or AP lumbar diameters rather than wedging, because these are simultaneous equations. What is important is that there exists an inverse relationship between VNC and degree of wedging. The independent variables were age, sex, culture, nerve root tunnel distance, and severities of vertebral osteophytosis.

In the first equation, controlling for age, sex, culture, nerve root tunnel distance, and severity of vertebral osteophytosis, lumbar VNC TR diameters are significantly inversely correlated with wedging ($R = -0.26$, $P < 0.05$). The R^2 is significant ($R^2 = 0.18$, $P < 0.05$). The second equation considers the morphometric variables separately from the population parameters. Wedging is the only morphometric significantly (inversely) correlated with TR diameters ($R = -0.23$, $P < 0.05$), but R^2 is not significant.

The third equation controls for age, sex, culture, nerve root tunnel distance, and severity of vertebral osteophytosis. There is no significant relationship between lumbar VNC AP diameters and wedging. The fourth equation, which considers only the morphometrics, shows that wedging is significantly correlated with AP diameters ($R = -0.21$, $P < 0.05$). R^2 is also significant ($R^2 = 0.29$; $P < 0.001$).

In summary, these results suggest that poor early growth, reflected in small VNC, predicts significantly greater wedging in the adult (presumably indicative of bone loss) regardless of adult age, sex, diet (biocultural differences through time at Dickson), nerve root tunnel length, or degree of vertebral osteophytosis (osteoarthritis). Usually it is held that (adult) age, sex, and diet are considered preeminent in osteoporosis. This suggests that poor growth prior to early childhood may in fact be preeminent in producing osteoporosis in the adult.

Bone loss is accelerated with decreased health as a result of decreased physical activity and increased physiological stress. Thus, small canal size, as a result of poor early growth, does appear to generally predict decreased adult health.

TABLE 3. Standardized multiple regression: Lumbar vertebral neural canal diameters and wedging

Independent variables	Transverse diameters		Anteroposterior diameters	
	Beta weights		Beta weights	
	Eq. 1	Eq. 2	Eq. 3	Eq. 4
Age	0.15		0.14	
Sex			0.08	
1. Male	−0.34**			
2. Female				
Culture				
1. PreMiss.	−0.002		−0.32**	
2. Miss.				
Nerve root tunnel	0.12	0.13	0.56***	0.53***
Vertebral osteophytosis	0.02	0.10	−0.01	0.08
Wedging	−0.26*	−0.23*	−0.07	−0.21*
R^2	−0.18*	0.08	0.40***	0.29***

*P < 0.05.
**P < 0.01.
***P < 0.001.

TABLE 4. Lumbar and thoracic vertebral neural canal size: Alive vs. dead by age groups

Age	Status	n	X	SE	Prob < |t|
A. Lumbar segment transverse diameters					
15–25	Alive	59	22.70	0.18	0.03
	Dead	18	21.85	0.40	
25–35	Alive	41	22.82	0.20	n.s.
	Dead	18	22.66	0.42	
35–45	Alive	21	22.80	0.26	n.s.
	Dead	20	22.85	0.32	
45–55	Alive				
	Dead	21	22.80	0.26	
B. Lumbar segment anteroposterior diameters					
15–25	Alive	59	15.30	0.14	0.07
	Dead	18	14.57	0.34	
25–35	Alive	41	15.26	0.25	n.s.
	Dead	18	15.41	0.27	
35–45	Alive	21	15.44	0.38	n.s.
	Dead	20	15.07	0.34	
45–55	Alive				
	Dead	21	15.44	0.38	
C. Thoracic segment anteroposterior diameters					
15–25	Alive	55	15.62	0.14	0.05
	Dead	17	15.05	0.23	
25–35	Alive	41	15.80	0.15	0.02
	Dead	14	15.07	0.32	
35–45	Alive	21	15.90	0.23	n.s.
	Dead	20	15.70	0.18	
45–55	Alive				
	Dead	21	15.90	0.23	

Vertebral neural canal size and life-span

Table 4 compares lumbar segment VNC TR and AP diameters for individuals alive and those dead at each age period (15–25, 35–45, etc.) by means of t tests. Results for the lumbar (Table 4A) segment shows that individuals dying in the 15–25 age group had significantly smaller VNC TR diameters than survivors ($P < 0.03$). Table 4B shows that for individuals dying within the 15–25 age-at-death group VNC AP diameters approach being significantly smaller than those of survivors ($P < 0.07$). All other comparisons are not significant.

Analysis for the thoracic segment (Table 4C) showed that individuals dying in the 15–25 ($P < 0.05$) and 25–35 ($P < 0.02$) age groups had significantly smaller VNC AP diameters than those of survivors. After age 35 no other comparisons were significant, nor were there even tendencies. No TR diameters were significant according to t tests.

Individual analysis for thoracic vertebrae (Fig. 5A,B) showed that in the 15–25 age group, 7 of 12 VNC AP diameters, according to t tests, were significantly smaller in the dead than in survivors. T5 values also tend to approach significance ($P < 0.07$).

Of 12 VNC AP diameters 11 (at least) tend to be smaller in the dead than in survivors. A sign test shows that this tendency is significant ($P < 0.005$). In the dead 11 of 12 VNC TR diameters tend to be smaller than in survivors ($P < 0.005$).

In the lumbar vertebrae (not shown) 4 of 5 VNC TR diameters were significantly smaller, within the 15–25 age group, and L5 values tended to be smaller than in survivors. Among the VNC AP diameters none were significantly smaller, but all 5 tended to be smaller. Sign tests could not be performed, because at least six groups were necessary for such tests (Thomas, 1976).

Overall, for combined lumbar and thoracic VNC AP and TR diameters within the 15–25 age group, of 34 diameters at least 32 (at least) tend to be smaller than in survivors. This tendency is significant ($P < 0.00001$). These parametric and nonparametric test results suggest that small VNC are significantly associated with decreased life-span, especially the thoracic AP VNC.

Growth disruption that occurs earliest is generally thought to have widest effects on health. We have suggested that features developing later are less reliable in predicting subsequent poor health, because they may more readily experience catch-up growth and may mask poor early neural and thymolymphatic growth.

This seemed to hold for VNC versus VH. However, it also seemed to hold even within the VNC. Lumbar TR VNC, although also

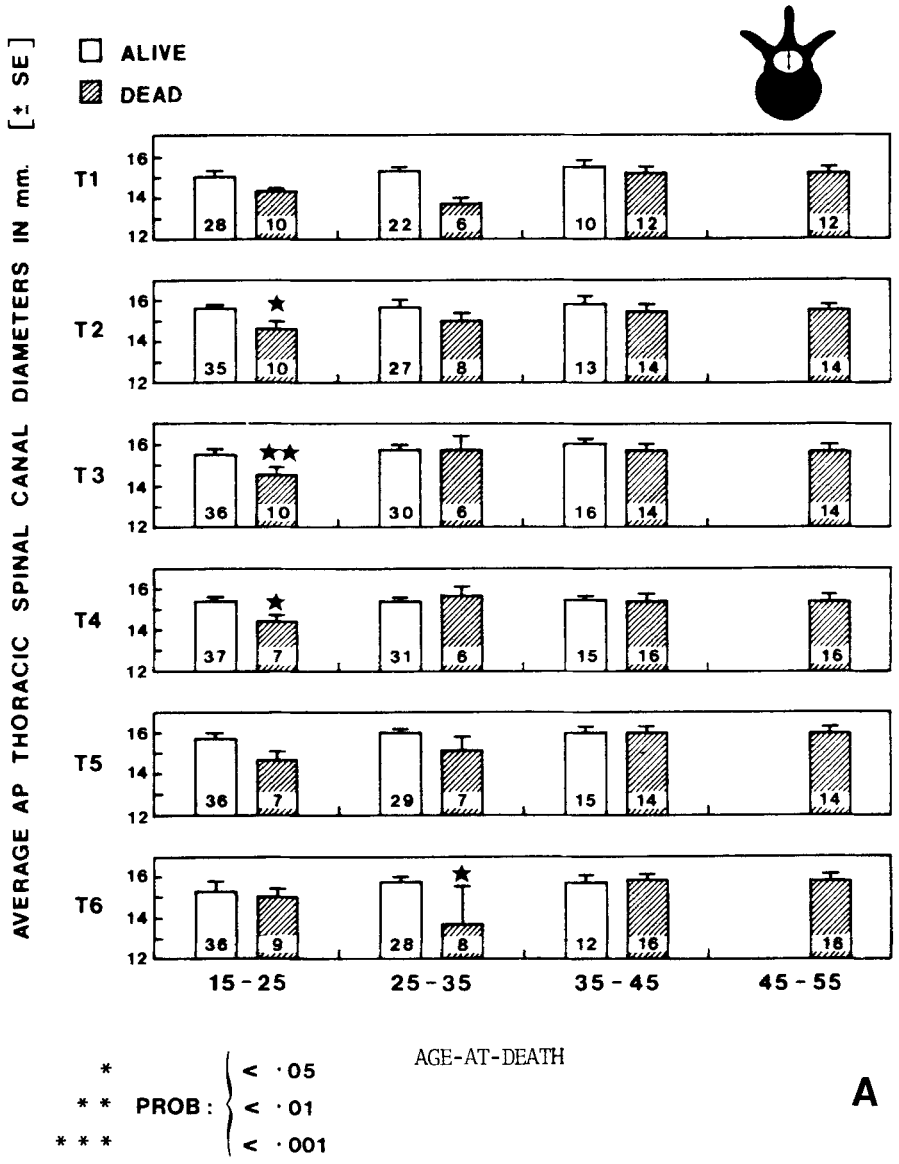

Fig. 5A. Individual average anteroposterior thoracic spinal canal diameters (in mm), T1–T6.

showing a significant tendency to be smaller in those with younger adult-age-death, were generally the weakest VNC diameters in association with decreased adult life-span. On the other hand, thoracic AP VNC were the most highly associated with younger adult age-at-death, and they develop earliest, completely in utero.

Multivariate analysis for VNC diameters and life-span was not conducted, because of the apparently nonlinear relationships across the age groups. Multivariate analysis within age groups was impossible owing to their small sample sizes.

DISCUSSION

One alternative hypothesis is that females died more frequently than males in the younger age-at-death group, perhaps in childbirth. If females normally had smaller VNC than males, this traumatic death would have led to the spurious conclusion that small

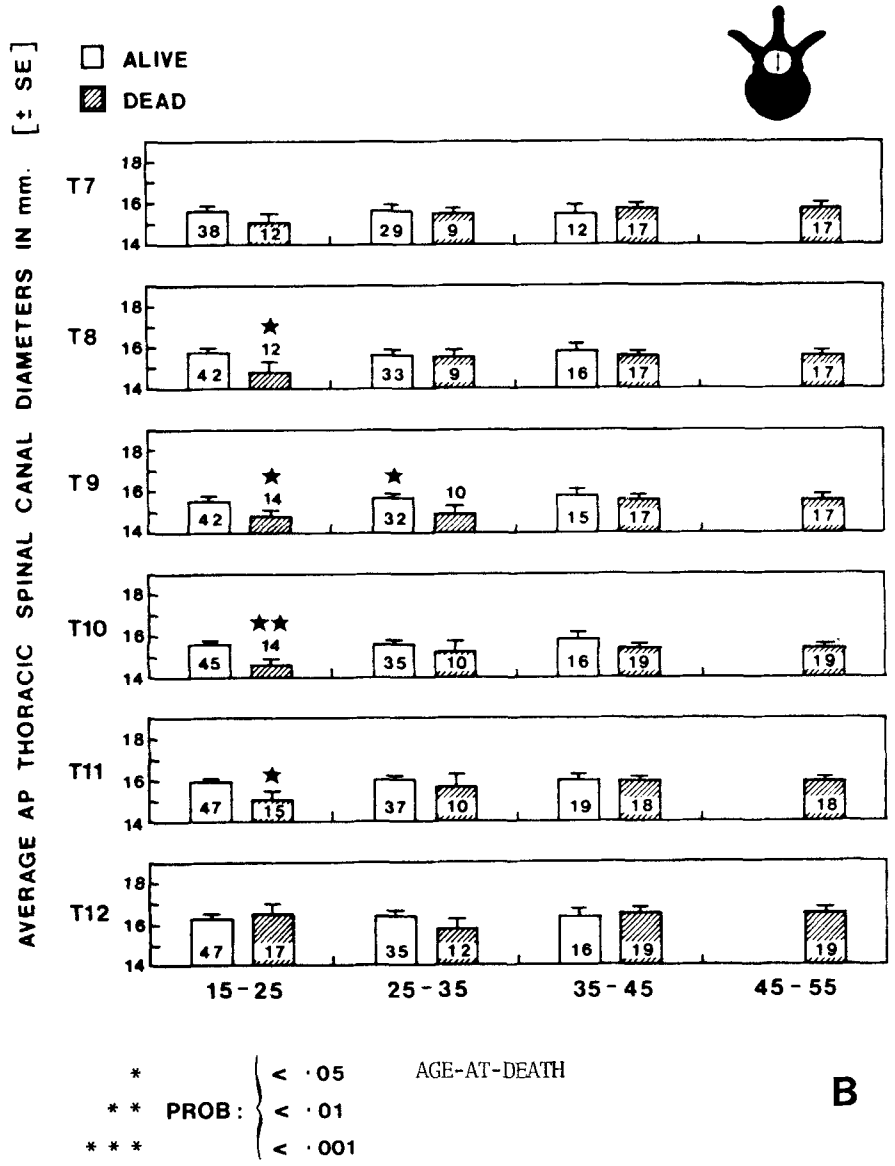

Fig. 5B. Individual average anteroposterior thoracic spinal canal diameter (in mm), T7–T12.

VNC were associated with decreased lifespan. However, there were no significant differences in thoracic or lumbar VNC AP and TR diameters between the sexes in either the 15- to 25-year or 25- to 35-year age-at-death group. For fuller explanation of sexual dimorphism and VNC in Dickson populations see Clark (1985,1986).

Another potential problem with this analysis is that in adult skeletal material it is difficult to distinguish between small VNC and stunted VNC. (Even so, our results would still stand.) However, it appears that individuals in the youngest age-at-death groups actually have stunted, rather than merely small, VNC. For example, in the youngest age-at-death groups (15–25 years) VNC are independent of VH. (TR:$r = -0.00$, n.s., $n = 18$; AP: $r = 0.38$, n.s. $= 18$). Thereafter, VNC and VH are dependent. This relationship is stronger in the older age-at-death groups and strongest in the 45–55 (oldest) age group (TR:

$r = 0.60$, $P < 0.01$, $n = 21$; AP: $r = 0.46$, $P < 0.05$, $n = 21$). This suggests that individuals who experienced stunted growth in early childhood (and small VNC) also suffered permanently impaired neural and immunological function. Yet this stress was not severe, because they survived until adulthood, and apparently caught up in respect to VH. VNC and VH were dependent in the older groups, because no stunting in early growth occurred (and there was strong positive allometry between VNC and VH, and these individuals lived the longest).

Similar results show that poor early growth may permanently stunt features that mature early and be associated with neurological dysfunction but that those maturing late do not reflect poor early growth. For example, Stoch and Smythe (1976) found that populations that survived infant malnutrition in consequence of nutritional supplements commencing in childhood caught up by adulthood in weight and height, but, compared to controls, they remained significantly stunted in head circumference (HC) and neurological function because nutrition intervention commenced at age 6 after HC ceased growth (about age 4) (see also Brandt, 1978). This is analogous to the stunted VNC and apparently normal VH in the younger adult age-at-death groups.

Eisenstein (1983) compared VNC and VH between South African white and black skeletons. Vertebral neural canals were significantly smaller in the blacks than in the whites, but there was no difference in VH. He ascribed this phenomenon to genetic differences between these populations. We suggest that blacks had poorer infant health than whites, but by adulthood blacks caught up in VH, while remaining stunted in VNC.

Stunted development prior to early childhood, rather than small size, appears to be correlated with decreased adult health and life-span because neither tibial length nor VH (i.e., statural components) was associated with these conditions. This also suggests that poor early growth and adult health is best measured on the basis of features that complete their growth early. Ironically, such auxological investigations primarily focus on stature or weight.

Initially it would seem that wedging is a poor way to measure bone loss and general health status. However, vertebral wedging is a widely used clinical measure of bone loss (e.g., Riggs et al., 1982; Giansiracusa and Kantrowitz, 1982; Guggenheim et al., 1971) and general health status (see Clark, 1985). Although the exact shape change that occurs in vertebrae with age is problematic, all vertebrae decline significantly in height and become significantly broader with aging or disease (Ericksen, 1976; Arnold et al., 1970).

Interestingly, both Milne and Lauder (1976) and Arnold et al. (1970) suggest that bone loss in the vertebral body is greater in the anterior than the posterior portion of the vertebral body, leading to asymptomatic microfracture and vertebral collapse. The rectangularly shaped vertebral bodies generally become wedge-shaped with age (and presumably certain diseases).

Our study shows similar results to those above. Results here suggest that better early growth (larger VNC) produced increased anterior vertebral body height (skeletal mass) in adults (AP: $r = 0.28$, $P < 0.01$, $n = 87$; TR: $r = 0.29$, $P < 0.01$, $n = 87$). However, there was no relationship between VNC and the posterior vertebral body height (AP: $r = 0.12$, n.s., $n = 87$; TR: $r = 0.10$, n.s., $n = 87$). Thus, poor early growth does indeed appear to have significant impact on size (skeletal mass) of the anterior vertebral body heights, but there was relatively little affect between VNC (poor early growth) on the posterior vertebral body heights. Hence, a relationship between small VNC and vertebral wedging exists, but there is no relationship between small VNC and shorter trunk length (i.e., stature).

It is now recommended that cancellous bone density be used to assess bone loss (American College of Physicians, 1983), because it is far more sensitive than cortical bone to metabolic and mechanical stress. Among cancellous bone sites vertebrae appear to be the most sensitive indicators of bone loss (Pogrund et al., 1979). Vertebrae are over 90% cancellous bone with four times more bone surface area exposed to blood than cortical bone. This increases the potential dissolution of bone (Frost, 1973).

Unfortunately, in archeological populations it is difficult to precisely measure cancellous bone. Cancellous bone is easily lost because of postmortem factors such as weathering. Fortunately, the cortical shell surrounding the vertebral body (composed of the cancellous bone) is stable. As a result, measuring wedging of the cortical shell (vertebral heights) provides inference in respect to

cancellous bone loss, because the cortical shell collapses only after more extensive cancellous bone loss within the vertebral body (Milne and Lauder, 1976). Thus, our correlations between poor early growth and wedging are probably conservative estimates of the actual relationships between poor early growth and cancellous bone density and loss.

Two mechanisms are usually given to explain osteoporosis: 1) decreased skeletal mass at maturity that is due to impaired formation, and 2) the rate of bone loss (e.g., Giansiracusa and Kantrowitz, 1982). Perhaps individuals with poor early growth have small VNC, decreased skeletal mass (especially in the anterior portion of the vertebrae), and impaired neural and immune function. This would further accelerate bone loss due to decreased physical activity and increased physiological stress (i.e., decreased health).

Deficits of bone mineral, as a result of impaired early growth, may not show up as clinically significant disease until a threshold is reached in adulthood when these subclinical deficits are compounded by normal age-related bone loss commencing at skeletal maturity. A similar suggestion has been made as to the cause of immunodeficiency diseases that occur with adult aging.

In a review of immunodeficiencies and aging, Makinodan (1980) suggested that what is not known is whether immunodeficiency diseases, normally associated with aging, compromise immune function or whether the decline with age in immune functions crosses a threshold level that predisposes adults to eventual disease. He supports the latter view, because the onset of the decline in immune functions occurs when the thymus begins normally to involute in adolescence (or the cortex at birth). Thus he suggests that normal thymic involution may be a single, dormant, underlying central mechanism responsible for the loss of immunological vigor with age.

We propose that stunted neural and immune development (SNID) and function that occur before early childhood might explain some of the considerable variation (accelerated aging) found between individuals and populations in neural and immunodeficiency diseases and life-span. Moreover, such stunting may be common in affluent and especially in poor modern industrial populations and underdeveloped countries. Although most of the relevant work has been done in severely malnourished populations, a variety of stressors are known to influence prenatal and early postnatal growth (see McCormick, 1985). For example, maternal smoking produces significantly reduced infant head circumference (D'Souza et al., 1981) and decreased weight through 7 years of age (Garn et al., 1978). Other sources of maternal and/or fetal stress (that may produce SNID) include hypertension, alcohol use, placental insufficiency, climate, and airport noise. Worldwide, the most common problem is malnutrition. What happens to neurological and immunological function?

There are several studies both in prehistoric and in modern industrial populations that have consistently shown that early stunted growth results in disease and decreased life-span in adults. For example, in prehistoric populations individuals dying in late adolescence had significantly smaller tooth size than did those surviving until adulthood (Guagliardo, 1982). Similarly, disrupted dental enamel development is significantly associated with decreased life-span in adults from Dickson Mounds (Rose et al., 1978). Disrupted enamel development has also been found in skeletons of younger age-at-death from modern industrial samples, and the cause of death was most often infectious and neurological diseases (Goodman, 1985). In modern living populations, disrupted enamel development has been frequently found in individuals with minimal (Bergman et al., 1965), as well as extreme (Martin et al., 1960) neurological diseases.

Estimates of the adult physique in modern populations, which use stature as a shape component, have been inconsistently associated with decreased adult health and abnormal physiological functions, including eosinophil count (Burr and Damon, 1970; Rud, 1947), endocrine function (Bridges and Jones, 1973), cancers (Westphal et al., 1979; McWhirter et al., 1983), bone loss (Hansson and Roos, 1980), and diabetes (Mueller et al., 1984). Early physiological stress may cause increased adult stature (Clark, 1985), but those features that complete their growth before this period are generally stunted in development even in the adult. To date no study has proposed a causal mechanism that explains why features completing their growth early in development, not in adulthood, are most predictive of adult disease and de-

creased life-span. We propose that SNID, as indicated by small VNC, may be of some importance in understanding the variability of neural and immune function that helps determine adult health and life-span.

CONCLUSIONS

Our results show that small vertebral neural canals (VNC) in both the anteroposterior and transverse diameters are significantly correlated with greater vertebral wedging (bone loss), even after age, sex, culture, nerve root tunnel distance, and vertebral osteophytosis are controlled. Thus, the importance of age, sex, and culture in predicting wedging (bone loss) appears to be outweighed by poor growth prior to early childhood. Perhaps the current attempts to prevent bone loss, often commencing after adulthood, are too narrowly focused.

Individuals with small VNC TR and AP diameters also have a significantly reduced life-span (adult age-at-death). Vertebral neural canals are potentially independent of vertebral height and tibial length. This suggests that stature in the adult may mask poor early growth, as well as the relationship between poor early growth, adult health, and life-span.

Since this research in prehistoric populations was completed, independent researchers have confirmed this model in four modern urban industrial populations (Porter, 1985). Specifically, VNC were measured in vivo, using ultrasound, in several hundred adolescents and adults. The study design was longitudinal (retrospective) and individuals were randomly sampled. Individuals with smaller VNC compared to population normals had significantly (t test, $P < .05 - .01$): 1) greater somatic complaints, 2) greater psychological depression, 3) poorer standardized test scores through high school, 4) more infections, and 5) higher absenteeism on the job. More recent research also suggests that our model of stunted neural-immune development is correct. For example, Wilson et al (1985) found that low birth weight in infants, due to such prenatal stressors as hypoxia, leads to phenotypically less mature circulating B and T cells. This results in impaired immune function.

Small VNC is known to be a principle cause of (idiopathic) back ache (Porter et al. 1980). Clark et al. (1985) suggested that this component of back ache may be developmental. Our results here suggest a general clinical significance of small VNC beyond the importance of back ache.

Low birth weight and fetal growth retardation, due to such factors as maternal malnutrition or psychological stress, are now generally recognized in underdeveloped and developed countries as important factors that predict perinatal and infant mortality, as well as learning disabilities in children. The acute and chronic disabilities come at great personal and social cost (McCormick, 1985).

If further research upholds the premise that poor early growth, even of seemingly minor magnitude, actually predicts lifelong compromised health, then the social and personal costs of poor early growth have been greatly underestimated. Currently, these costs are calculated from disability through childhood and not adulthood. At present it appears that improving early growth prior to early childhood may be critical to maximizing health and life-span in the adult.

ACKNOWLEDGMENTS

This research was supported by NIH Biomedical Research grant No. 632-509 and a Smithsonian Postdoctoral Fellowship awarded to G.A. Clark. We thank Bob Gylnn, Don Taylor, Ryan Bliss, Tom Matte, and Bill Stini for their editorial advice.

LITERATURE CITED

American College of Physicians (1983) Recommendation: Radiologic Methods to Evaluate Bone Mineral Content. Clinical Efficacy Assessment Project. Philadelphia: ACP pp. 1–8.

Arnold, JS, Wei, J, Cochran, T, Ament, C, McNeill, G, and Gitta, P (1970) External and trabecular morphologic changes in lumbar vertebrae in aging. In Second Conference of Bone Mineral Measurements. Bethesda, MD: National Institutes of Health, pp. 352–402.

Bass, WM (1971) Human Osteology. Missouri Archaeological Society, Inc., Special Publications. Columbia, MO: University of Missouri, p. 187.

Barson, AJ (1974) Developmental pathology of the spine. In JA Davis and J Dobbing (eds): Scientific Foundations of Pediatrics. Philadelphia: JB Saunders, pp. 759–785.

Bergman, G, Bille, B, and Lyttkens, G (1965) Tooth ring analysis in minimal brain dysfunction. Lancet *1*:963.

Blakey, ML, and Armelagos, GJ (1985) Deciduous enamel defects in prehistoric Americans from Dickson Mounds: Prenatal and postnatal stress. Am. J. Phys. Anthropol. *66*:371–380.

Boyd, E (1936) Weight of the thymus and its component parts and number of Hassal corpuscles in health and disease. Am. J. Dis. Child. *51*:313–335.

Brandt, I (1978) Growth dynamics of low-birth-weight infants with emphasis on the perintal period. In F Falkner and JM Tanner (eds): Human Growth and Postnatal Growth. New York: Plenum, pp. 557–617.

Bridges, PK, and Jones, MT (1973) Relationships be-

tween some psychological assessments, body-build, and physiological stress responses. J. Neurol. Neurosurg. Psychiatry. *36*:839–845.

Brooke, OG, Wood, C, and Butters, F (1984) The body proportions for small-for-date infants. Early Hum. Devel. *10*:85–94.

Burr, WA, and Damon, A (1970) Physique and the eosinophil count. Hum. Biol. *42*:202–205.

Clark, GA (1985) Heterochrony, Allometry, and Canalization in the Human Vertebral Column: Examples From Prehistoric Amerindian Populations. Ph.D. Dissertation, Department of Anthropology, University of Massachusetts, Amherst; International Microfilms, Ann Arbor, #8509532.

Clark, GA (1986) Adult sexual dimorphism and status in prehistoric populations. Am. J. Phys. Anthropol. 69:187–188 (abstract).

Clark, GA, Panjabi, MM, and Wetzel, FT (1985) Can infant malnutrition cause adult vertebral stenosis? Spine, *10*:165–170.

Cohen, J, and Cohen, P (1975) Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences. New Jersey: Lawrence Erlbaum, pp. 3–72.

Cruess, RL (1982) The effects of corticosteroirds on the musculoskeletal system. Ann. RCPSC *15*:485–494.

D'Souza, SW, Black, P, and Richards, B (1981) Smoking in pregnancy associations with skinfold thickness, maternal weight gain, and fetal size at birth. Br. Med. J. *282*:1661–1663.

Dubos, R, Schaedler, SW, and Costello, R (1969) Lasting biological effects of early developmental influences. Conditioning of adult size by prenatal and postnatal nutrition. J. Exp. Med. *127*:783–799.

Eisenstein, S (1983) The morphometry and pathological anatomy of the lumbar spine of South African Negroes and Caucasoids with specific reference to spinal stenosis. Spine *8*:187–191.

Ericksen, ME (1976) Some aspects of aging in the lumbar spine. Am. J. Phys. Anthropol. *51*:563–570.

Fabris, N (1977) Hormones and aging. In T Makinodan and E Yunis (eds): Comprehensive Immunology. I: Immunology and Aging. New York: Plenum, pp. 73–89.

Ford, GW, Belbin, R, Jose, DG, Vorbach, EA, and Kirke, DK (1976) Growth and immune function in aboriginal children during recovery from malnutrition and infection. Aust. N.Z. Med. *6*:321–328.

Frost, HM (1973) The spinal osteoporosis mechanisms of pathogenesis and pathophysiology. Clin. Endocrinol. Metab. *2*:257–275.

Garn, SM, Shaw, HA, and McCabe, KD (1978) No ifs, ands or butts: An essay on the maternal smoking effect. In R Schemmel (ed): Symposium on Human Nutrition. Research Report 364, Michigan State University.

Giansiracusa, DF, and Kantrowitz, FG (1982) Osteoporosis. In Rheumatic and Metabolic Bone Diseases in the Elderly. Lexington, MA: Collamore, pp. 169–179.

Gisler, RH, Bussar, AF, Maxie, JC, and Hess, R (1971) Hormonal regulation of the immune response. I. Induction of an immune response in vitro with lymphoid cells from mice exposed to acute systematic stress. Cell Immunol. *2*:69–634.

Goodman, AH (1985) Childhood dental hypoplasias predictors of adult mortality in an industrial population. Am. J. Phys. Anthropol. (abstracts) *66*:175.

Goodman, AH, Lallo, J, Armelagos, GJ, and Rose, JC (1984) Health changes at Dickson Mounds, Illinois (A.D. 950–1300). In MN Cohen and GJ Armelagos (eds): Paleopathology at the Origins of Agriculture. New York: Academic, pp. 271–305.

Guagliardo, MF (1982) Tooth crown size differences between age groups: A possible new indicator of stress in skeletal samples. Am. J. Phys. Anthropol. *58*:383–389.

Guggenheim, K, Reshef, A, Ben-Menachem, V, and Bernstein, DS (1971) An epidemiological study of osteoporosis in Israel. Arch. Environ. Health *22*:259–264.

Hammar, JA (1909) Fümzig Jahre Thymusforschung. Ergeb. Anat. Entwicklungzsgesch. *19*:1.

Hammar, JA (1921) The new views as to the morphology of the thymus gland and their bearing on the problem of the functions of the thymus. Endocrinology *5*:543–573.

Hansson, T, and Roos, B (1980) The influence of age, height, and weight on the bone mineral content of lumbar vertebrae. Spine *5*:545–551.

Harn, AD (1974) Cahokia and the Mississippian emergence in the Spoon River area of Illinois. Trans. Ill. State Acad. Sci. *68*:414–434.

Harn, AD (1984) (Unpublished data). Illinois State Museum. Springfield, Illinois.

Haynes, BF (1984) Phenotypic characterization and ontogeny of components of the human thymic microenvironment. Clin. Res. *32*:500–507.

Hinck, VC, Clark, WM, and Hopkins, CE (1966) Normal interpediculate distances (minimum and maximum) in children and adults. Radiology *97*:141–153.

Jose, DG, Stutman, O, and Good, RA (1973) Long-term effects on immune function of early nutritional deprivation. Nature *241*:57–58.

Kendall, MD (1981) Introduction. In MD Kendall (ed.): The Thymus Gland. New York: Academic Press, pp. 1–6.

Lallo, M (1973) The Skeletal Biology of Three Prehistoric American Indian Societies from Dickson Mounds. Ph.D. Dissertation, Department of Anthropology, University of Massachusetts, Amherst.

Lamb, MJ (1977) Modifying the rate of ageing and the length of life. In Biology of Ageing. New York: John Wiley, pp. 73–89.

Makinodan, T (1980) Immunodeficiencies and ageing. In G Doria and A Eshkol (eds): The Immune System Functions and Therapy of Dysfunction. New York: Academic, pp. 55–63.

Maresh, MM (1970) Measurements from roentgenograms, head size, long bone lengths, bone muscles and fat widths, skeletal maturation. In RW McCammon (ed): Human Growth and Development. Springfield, Illinois: C.C. Thomas, pp. 155–200.

Martin, JK, Thompson, MW, and Castaldi, CR (1960) A study of clinical history, tooth enamel, and dermal patterns of cerebral palsy. Guy's Hospital Rep. *109*:139.

McCormick, MC (1985) The contribution of low birth weight to infant mortality and childhood morbidity. N. Engl. J. Med. *312*:82–89.

McGillis, JP, Hall, NR, and Goldstein, A (1983) Circadian rhythm of thymosin-alpha 1 in normal and thymectomized mice. J. Immunol. *131*:148–151.

McWhirter, WR, McWirter, KM, and Taylor, D (1983) Height and lymphoblastic leukemia. Arch. Dis. Child. *58*:839–840.

Miller, CL (1978) Immunological assays as measures of nutritional status: A review. J. Parenter. Enteral Nutr. *2*:554–566.

Milne, JS, and Lauder, IJ (1976) The relationship of kyphosis to the shape of vertebral bodies. Ann. Hum. Biol. *3*:173–179.

Mueller, WH, Joos, SK, Hanis, CL, Zavaleta, AN, Eichner, J, and Schull, WJ (1984) The diabetes alert study: Growth, fatness, and fat patterning, adolescence through adulthood in Mexican American. Am. J. Phys.

Anthropol. *64*:389–399.

Mugerwa, JW (1971) The lymphoreticular system in kwashiorkor. J. Pathol. *105*:105–268.

Nathan, H (1962) Osteophytosis of the vertebral column. J. Bone Joint Surg. *44A*:243–268.

Panjabi, MM, Takata, K, and Goel, VK (1983) Kinematics of lumbar intervertebral foramen. Spine *8*:348.

Pierpaoli, W (1981) Integrated phylogenetic and ontogenetic evolution of neuroendocrine and identity-defense, immune functions. In R Arden (ed): Psychoimmunology. New York: Academic, pp. 575–606.

Pierpaoli, SA, and Sorkin, E (1972) Hormones, thymus, and lymphocyte functions. Experientia *28*:1385–1389.

Platt, BS, and Stewart, RJC (1962) Transverse trabeculae and osteoporosis in bones in experimental protein-calorie deficiency. Br. J. Nutr. *16*:483–495.

Pogrund, H, Makin, M, Robin, G, Menczel, J, and Steinberg, R (1979) Osteoporosis of the spine, pelvis and hand. Clin. Orthop. *139*:156–163.

Porter, RW (1985) Personal communication (Doncaster Royal Infirmary, Doncaster, England).

Porter, RW, Hibbert, C, and Wellman, P (1980) Backache and the lumbar spinal canal. Spine *5*:99–105.

Riggs, BL, Seeman, E, Hodgson, SF, Taves, DR, and O'fallon, WM (1982) Effect of the fluoride/calcium regimen on vertebral fracture occurrence in postmenopausal osteoporosis. N. Engl. J. Med. *306*:448–450.

Rose, JC, Armelagos, GJ, and Lallo, JW (1978) Histological enamel indicators of childhood stress in prehistoric skeletal samples. Am. J. Phys. Anthropol. *49*:511–516.

Rud, F (1947) The eosinophil count in health and in mental disease. Oslo: J.G. Tanum Forlag.

SAS Institute (1982) Users Guide: Statistics. Cary, North Carolina: SAS Institute.

Sellmeyer, EE, Bhettay, E, Trusswell, AS, Meyers, OL, and Hansen, JDL (1972) Lymphocyte transformation in malnourished children. Arch. Dis. Child. *47*:429.

Stoch, MB, and Smythe, DM (1976) Fifteen-year developmental study on effects of severe undernutrition during infancy on subsequent physical growth and intellectual functioning. Arch. Dis. Child. *51*:327–336.

Tannenbaum H (1984) Osteopenia in rheumatology practice and therapy *13*:337–348.

Thomas, DH (1976) Figuring Anthropology: First Principles of Probability and Statistics. New York: Holt, Rhinehart, and Winston, pp. 327–332.

Watts, T (1969) Thymus weights in malnutrition. J. Trop. Pediatr. *15*:155–158.

Westphal, M, Morgan, SK and Grush, OC (1979) Nutrition and growth in children with acute lymphoblastic leukemia (ALL). Clin. Res. *27*:81A.

Williams, JPG (1981) Catch-up growth. Embryol. Morphol. *65*:743–758.

Wilson, M, Rosen, FS, Schlossman, SF, and Reinheoz, EL (1985) Ontogeny of human T and B lymphocytes during stressed and normal gestation: Phenotypic analysis of umbilical cord lymphocytes from term and preterm infants. Clin. Immunol. Immunopathol. *37*: 1–12.

Winick, MJ (1969) Malnutrition and brain development. J. Pediatr. *74*:667–677.

Winick, M (1973) Relation of nutrition to physical and mental development. Nutr. Diet *18*:114–122.

Winick, M, and Noble, A (1966) Cellular response in rats during malnutrition of various ages. J. Nutr. *89*:300–306.

Zubiran, S, and Gomez-Mont, F (1953) Endocrine disturbances in chronic human malnutrition. Vitam. Horm. *11*:97–132.