Original Research Article

Sex Differences in Child Nutritional and Immunological Status 5–9 Years Post Contact in Fringe Highland Papua New Guinea

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Objectives: This study examines sex differences in vulnerability among children experiencing rapid culture change that may reflect distinct microecologies driven by differential parental investment and/or sex-specific life history strategies. Apparent female growth canalization may be a life history strategy favoring growth over maintenance but also may reflect sex-differentiated selection for resilience based on unequal treatment during early life.

Methods: Stature, weight, and serum measures of C-reactive protein (CRP, an inflammation marker) and Epstein-Barr Virus antibodies (EBV, a humoral immune response marker) were collected longitudinally among children/adolescents ages 5–20 years (N = 65), 5–9 years after sustained contact in a fringe highland hunter-horticulturalist group from the Schrader Range in Papua New Guinea exhibiting male preference and sex-biased survival. It was hypothesized that girls would exhibit canalization, with better nutritional status than boys; lower maintenance investment would yield lower female immune activation; and because of differential survivorship, females would appear increasingly canalized as early conditions for girls worsened relative to boys.

Results: Girls had greater arm circumference z-scores than boys, less frequent stunting, and lower CRP despite high pathogen load. Average nutritional status for girls improved over time as the sex ratio became increasingly male biased and the condition of female infants reportedly worsened.

Conclusions: Both canalization and survivorship effects were found. Although a life history perspective on female canalization can help explain developmental outcomes in populations undergoing rapid culture change amid adversity, possible sex differences in the strength of survivorship effects that select for resiliency should not be ignored. Am. J. Hum. Biol. 00:000–000, 2010. © 2010 Wiley-Liss, Inc.

The convergence of unparalleled growth in net global wealth with profoundly unequal wealth distribution has intensified inequities within and among societies. Hence, identifying pathways toward vulnerability or resilience in the face of rapid global culture change is a major public health concern (Worthman and Kohrt, 2005). The comparative study of child growth under different rearing conditions has highlighted the importance to child well-being not only of historical, structural, and material factors at the population level but also of microecologies of individuals or subgroups of children within the same society and even within the same household (Bogin, 2001). In particular, culturally informed, sex-differentiated access to resources and patterns of exposure to disease foster sex differences in developmental trajectories that belie simple predictions based on conditions under which the group as a whole resides (Stinson, 1985; Worthman, 1996). Sex differences in developmental outcomes during culture change provide a case study in how localized forms of differential treatment intersect with variation in children’s intrinsic adaptive capacities. This study uses data collected among the Haga-hai of Papua New Guinea from 1988 to 1992, 5–9 years after sustained contact was established, to evaluate the role of female canalization and survivorship effects in sex-differentiated child growth outcomes.

Developmental trajectories can be modeled using life history theory, which concerns trade-offs between current and future reproduction given limited total energy available to invest in lifetime reproductive fitness (Bogin, 2001). A corollary is the need to balance the energetic costs of maintenance versus growth and development during the long lead-up to human reproductive maturation (Bogin, 2001; Worthman, 2003). Differential operation of life history trade-offs by sex may help to explain the empirical generalization that males are more sensitive than females to growth faltering under adverse conditions (Stinson, 1985). The limited female reproductive lifespan and greater obligation reproductive effort could create selective pressure to shift resources away from maintenance and toward growth, resulting in canalization of female growth trajectories to launch the reproductive career and ensure that a child could be successfully borne and breastfed.

Empirical evidence continues to be weakly supportive of female canalization on balance even while contrary examples emerge (Stinson, 1985). Growth rates are less variable among males than females across several small-scale societies (Walker et al., 2006). However, adult females in rural Mali under early life stress from malnutrition and disease are closer to U.S. standards than males (Dettwyler, 1992), and stunting is more severe among boys than girls in Sub-Saharan Africa and among the Makushi in Guyana (Wamani et al., 2007; Wilson and Bulkan, 2009). If females are canalized, their developmental trajectories should be less affected than among males by the adverse sequelae of culture change.

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Yet, survivorship effects also can shift population-level growth patterns (Ulijaszek, 2000), and sex-biased parental investment will yield discrepancies in how strongly each sex has been selected for resilience. If males are preferred, selection for female resilience will contribute to apparent female buffering or canalization at the population level; if females are preferred, the reverse is true. Consequently, assessing the respective roles of canalization and survivorship during culture change requires careful synthesis of multiple lines of data, including ethnographic reports regarding sex-differentiated parental care, sex ratios, and markers of child investment in growth and maintenance.

Immune markers have emerged as an effective means to quantify maintenance investment (McDade, 2003). For instance, the Epstein-Barr Virus (EBV) is a nearly ubiquitous herpesvirus that becomes permanently resident upon infection. In healthy populations, virus surveillance by the cell-mediated arm of the adaptive immune response is weakened during psychosocial stress, resulting in reactivation and a humoral (antibody) response (McDade et al., 2000). In a more ecologically challenged sample of Nepali children, however, EBV was elevated among those in better physiological condition. This may mean that high EBV under adverse conditions reflects resilience rather than stress, given sufficient energetic resources to mount a robust humoral response (Worthman and Panter-Brick, 2008). Hence, children who prioritize maintenance over growth should have higher EBV antibody levels.

Similarly, the acute phase proteins C-reactive protein (CRP) and α1-antichymotrypsin (ACT) are mediators of inflammation and markers of infectious disease load (McDade et al., 2008; Panter-Brick et al., 2001; Worthman and Panter-Brick, 2008). McDade et al. (2008) found among 2–4-year-old ‘Tsimane’ children of Amazonian Bolivia that slight elevation of CRP predicted reduced growth velocity over the subsequent 3 months compared to controls, likely reflecting the trade-off between maintenance and growth. High ACT and/or CRP also have been associated with stunting or growth faltering in 10–14-year-old Nepali boys and in The Gambia (Lunn, 2000; Panter-Brick et al., 2001), and there is a well-documented synergistic relationship between undernutrition and infectious disease in the etiology of growth faltering (Ulijaszek, 2000). Hence, acute phase proteins reflect increased maintenance effort in response to intense pathogen loads as energetic resources are directed toward mounting an inflammatory response.

A fortuitous opportunity to study human biology in the context of rapid cultural change comes from data collected over the late 20th century in Papua New Guinea (PNG), where ecologically and culturally diverse societies experienced intensive contact with outsiders late by global standards. The documentation of this process has allowed researchers to test evolutionary and biocultural implications of changes in resource distribution, ideology, and social structure (Alpers and Attenborough, 1992). Because of remote geography and self-isolation, until the 1980s, the Hagahai were a seminomadic hunter-horticulturalist group in the fringe highlands of PNGs Schrader Range, only minimally and indirectly influenced by missionaries and the central government. Following the initiation of sustained contact in 1983, researchers from the Papua New Guinea Institute for Medical Research (PNG IMR) described extremely high disease burden and infant mortality rates (IMRs), cultural preference for males, a male-biased sex ratio, and sex-differentiated morbidity and mortality favoring males (Jenkins, 1987; Jenkins, 1988; Jenkins et al., 1989). Yet, child developmental outcomes beyond 4 years post contact remain largely unexplored.

Data from this later, transitional period offers a unique opportunity to explore the emergence of sex-differentiated developmental trajectories in the face of sustained, rapid culture change, as the immediate perturbation caused by contact began to settle toward the longer term epidemiological and social transitions expected based on other modernizing populations in PNG and around the world (Alpers and Attenborough, 1992; Armelagos et al., 2005).

Hence, in this analysis, we aim first to describe the physical condition of Hagahai children and adolescents during the middle post contact period (5–9 years post contact, 1988–1992), using anthropometric and serological markers of nutritional and immunological status. We also consider trends in child well-being across the middle post contact period. We expect that children or adolescents of both sexes and at all ages continued to show high levels of stunting, poor current nutritional status, and levels of immune activation consistent with high infectious disease load. However, previously reported reductions in crude death rate (CDR) and IMR from 1985 to 1992 (Worthman et al., 1993) lead to the hypothesis that conditions were gradually improving, as aid programs began to mitigate some of the harmful effects of post contact epidemic disease.

Second, we consider what drove sex-differentiated responses to adverse conditions. If female growth was canalized as a result of their distinct life history strategy, we expect that constrained energetic resources shifted from maintenance toward achieving adequate growth for attaining reproductive maturation. Therefore, we predict that females displayed better growth and nutritional status than males but relatively muted immune system activation. Moreover, given reportedly male-biased sex ratios, a survivorship effect may have operated, wherein females were subject to a stronger selective filter than males. If so, surviving girls will have been taller for their age than males with better and less seasonally variable current nutritional status. Further, mean growth status among females beyond the ages of peak mortality may paradoxically have improved as conditions worsened for female infants relative to males.

BACKGROUND

During the study period, the Hagahai comprised five territorial groups of 20 to 95 people (250–300 total population), occupying the fringe highlands of the Schrader Range along the rugged border region of Madang, Enga, and Western Highland provinces (elevation 200–2,400 m) (Jenkins et al., 1989; Melliger, 2000). They subsisted primarily as seminomadic hunter-horticulturalists, relying on wild plant foods and hunting while using lightly tended gardens to fill dietary gaps. In late 1983, a group of Hagahai traveled to Mount Hagan to request trade goods and medical assistance, breaking a long history of isolation, and by the end of the following year both missionary and government presence in Hagahai territory were permanently established (Boyd, 1996; Jenkins et al., 1989). Nevertheless, through 1992, the area remained reachable only by helicopter or by lengthy and arduous treks on bush trails (Melliger, 2000).

Intense pathogen pressure both preceded and followed formal contact (Jenkins, 1987; Jenkins, 1988; Jenkins, 1996).
et al., 1989). Major endemic or epidemic diseases afflicting the population included malaria, influenza, diarrheal diseases, Hepatitis B, and Bancroftian filariasis (Jenkins, 1988). A well-equipped rural aid station was established in Hagahai territory at Yilu (Ilu), and widespread vaccination campaigns undertaken. However, travel by disease carriers into Hagahai territory and growing Hagahai settlements near mission bases exacerbated disease transmission (Jenkins et al., 1989; Melliger, 2000). Hence, medical efforts within the first 4 years did not substantially improve Hagahai health status (Jenkins, 1988; Jenkins et al., 1989).

During the first 3 years after contact, the Hagahai had a crude birth rate (CBR) of 38 and a CDR of 51 per 1000 (Jenkins, 1988). From 1988 to 1992, CDR improved to 41, whereas CBR declined to 30, indicating a healthier but still shrinking population (Worthman et al., 1993). Infant mortality was 568 per 1,000 from 1984 to 1987, exacerbated by well-documented cases of infanticide (Jenkins, 1988; Jenkins et al., 1989), but declined to 323 per 1,000 from 1988 to 1992 (Worthman et al., 1993). Although overt infanticide was largely eliminated following threats of legal action by missionaries, the practice may have continued covertly in the form of selective infant neglect (Jenkins, 1988; Jenkins and Milton, 1993).

A male-biased sex ratio from birth until age 20, higher prevalence of wasting among girls than boys under age 5, and higher mortality among female infants suggest that infanticide and severe early neglect were directed preferentially toward females (Jenkins, 1988; Jenkins and Milton, 1993; Worthman et al., 1993). Multiple lines of ethnographic evidence also suggest a preference toward males, including reports that Hagahai would wait longer to bring girls than boys to health care workers (Worthman et al., 1993) that female subsistence contributions were under-valued (Jenkins, 1988; Jenkins and Milton, 1993) and that unlike neighboring groups there was no tradition of paying bride price (Jenkins et al., 1989).

Male preference may have intensified during the period represented by the present data (Carol Jenkins, personal communication 6/92), due to the greater ability of males to engage in the cash economy (Jenkins, 1988; Jenkins et al., 1989; Melliger, 2000). Moreover, worsening nutritional status among females under 5 contrasted with improving nutritional status among males from 1985 to 1992 (Jenkins and Milton, 1993; Worthman et al., 1993).

METHODS

Data for this study were collected during five separate visits to Hagahai territory by PNG IMR personnel between December 1988 and July 1992. During each visit, serum was collected from males and females aged 5 to 20 years, to yield a total pool of 152 samples from 65 individuals. Nearly every child aged 5–20 is represented at least once in this pool, although population mobility caused incomplete subsamples from individual visits. Participant ages were estimated using an events chronology combined with birth sequence and physical exam. Because there was no universally known datable event before 1983, relative ages are more certain than absolute ages, and ages for younger children may be more accurate.

**Anthropometrics**

Height, weight, and arm circumference (AC) were measured by Jenkins or trained PNG IMR staff with a Holtain Harpenden stadiometer, a double beam field scale calibrated on site by weight addition, and a narrow metal tape (Frisancho, 1990). Z-scores of height for age (HAz) and body mass index for age (BMIz) were calculated using Epi Info 3.5.1 (CDC, Atlanta GA) based upon CDC 2000 growth charts (Kuczmarski et al., 2000). AC for age (ACz), which is not available from CDC charts, was calculated using NHANES I and II data tabulated by Frisancho (1990).

**Serum collection, storage, and assays**

Blood samples were obtained from the antecubital vein by venipuncture performed by a physician or medical technologist. Samples were allowed to clot at room temperature, spun on a field centrifuge, aliquotted to cryovials, and frozen in liquid nitrogen for storage and transport from the field. Samples were stored in PNG IMR at −23°C until shipment on dry ice to the Laboratory for Comparative Human Biology at Emory University, where they were stored at −26°C until assay, which occurred 7–11 years after initial collection and freezing.

The ELISA for Anti-EBV VCA p18, and its rationale, are detailed elsewhere (McDade et al., 2000). This study differs in the use of serum rather than dried blood spot samples. Briefly, using a commercially available kit from Diasorin (Stillwater MN; catalog #7590), VCA p18-coated wells were incubated first with samples, controls, and standards in duplicate, then with goat anti-human IgG conjugated with horseradish peroxidase (HRP). Wells were developed in the presence of tetramethylbenzidine and read at 450 nm. Intra-assay CVs were 1.7% for the low control (M = 55.7 A.U.) and 3.9% for the high control (M = 147.9 A.U.); inter-assay CVs were 3.8 and 4.6%. Persons below 25 A.U. are seronegative so their values are not informative of immunologic stress. Three of 152 observations fell below 25 A.U. and are omitted from analysis.

The ELISA for CRP (Dako Corporation, Carpinteria, CA) also is detailed elsewhere (McDade et al., 2000). Wells coated with rabbit anti-human CRP antibodies were incubated first with samples, controls, and standards in duplicate, then with rabbit anti-human antibodies conjugated with HRP. Wells were developed in the presence of OPD and read at 490 nm. Intra-assay CVs for the low (M = 9.8 mg/L), medium (M = 17.6 mg/L), and high (M = 33.7 mg/L) controls were 2.4%, 4.5%, and 1.3%; inter-assay CVs were 8.6%, 11.7%, and 13.2%.

**Data analysis**

Analyses were performed in SAS 9.1. The data are atypical in that they come from a nearly complete survey of an extremely small population. Any associations identified are unlikely to differ substantially from the population from which the sample was drawn as a result of random chance. Consequently, relations that are marginally significant at P < 0.10 are reported. These data require modeling procedures that account for repeated measures and that allow for individually variable number and timing of observations (Jiang, 2007). Restricted maximum likelihood estimation (REML), as implemented in SAS PROC MIXED, is appropriate for continuous dependent variables and unbalanced data. REML was used to test group differences in BMIz, HAZ, ACz, and LogEBV, to control for covariates, and to model changes across time. For
TABLE 1. Weight, height, arm circumference, and BMI by age for girls and boys

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>5–6.9</th>
<th>7–8.9</th>
<th>9–10.9</th>
<th>11–12.9</th>
<th>13–14.9</th>
<th>15–16.9</th>
<th>17–18.9</th>
<th>19+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>[14.4 ± 1.4]</td>
<td>17.4 ± 1.7</td>
<td>20.1 ± 1.6</td>
<td>24.7 ± 2.3</td>
<td>28.0 ± 4.1</td>
<td>36.9 ± 6.7</td>
<td>47.6 ± 7.0</td>
<td>48.2 ± 11.5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>107.8 ± 2.9</td>
<td>112.3 ± 3.4</td>
<td>122.7 ± 4.1</td>
<td>128.0 ± 6.7</td>
<td>140.9 ± 8.8</td>
<td>150.2 ± 7.2</td>
<td>152.1 ± 10.6</td>
<td></td>
</tr>
<tr>
<td>AC (cm)</td>
<td>[14.0 ± 1.7]</td>
<td>14.9 ± 1.4</td>
<td>15.8 ± 1.9</td>
<td>16.8 ± 1.1</td>
<td>17.5 ± 1.0</td>
<td>19.6 ± 1.9</td>
<td>22.8 ± 2.2</td>
<td>21.7 ± 3.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>15.4 ± 1.1</td>
<td>16.0 ± 0.9</td>
<td>16.3 ± 0.7</td>
<td>17.0 ± 1.1</td>
<td>18.4 ± 1.8</td>
<td>21.0 ± 2.1</td>
<td>20.0 ± 2.5</td>
<td></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>[16.4 ± 1.6]</td>
<td>[17.7 ± 2.8]</td>
<td>[22.8 ± 3.5]</td>
<td>23.7 ± 5.8</td>
<td>30.7 ± 7.2</td>
<td>40.4 ± 10.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>[116.6 ± 7.1]</td>
<td>[122.3 ± 8.5]</td>
<td>[132.7 ± 7.5]</td>
<td>141.2 ± 7.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC (cm)</td>
<td>[14.7 ± 0.8]</td>
<td>[14.7 ± 1.6]</td>
<td>[16.0 ± 1.7]</td>
<td>16.8 ± 2.1</td>
<td>18.7 ± 1.8</td>
<td>21.0 ± 2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>15.6 ± 1.6</td>
<td>17.2 ± 2.1</td>
<td>20.0 ± 4.1</td>
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<td></td>
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</tr>
</tbody>
</table>

All values are M ± SD, weighted by the number of observations per individual within each age range. Values are placed in brackets if fewer than 5 individuals were measured. No values are reported if fewer than three individuals were measured.

RESULTS

Sample retention

The number of individuals providing blood samples and anthropometric measures at least once between 60 and 130 months post contact is 65; the number of measurements included in this analysis is 152, for a mean of 2.32 measurements per individual, although 13 individuals (20% of the sample) were measured only once. At 60 months, n = 33; 84 months, n = 31; 90 months, n = 42; 97 months, n = 15; 103 months, n = 32.

To identify potential sources of biased attrition, an analysis was performed to determine whether growth or immunological status at the point of first measurement, between 60 and 97 months, predicts inclusion in the sample at 103 months. All individuals who were too old to have been included in the sample at 103 months (>20 years of age), or were first measured at 103 months, were excluded. Among those remaining (n = 51), using logistic regression, presence in the 103 month sample was not significantly predicted by sex, time or age of first measurement, age at 103 months, BMIz, HAz, ACz, stunting, or LogEBV.

However, the odds of being in the 103 month sample were 2.9 times higher among those with elevated CRP (CRP > 4), and extremely elevated CRP (CRP > 10). The test statistic used in PROC MIXED is the maximum likelihood F, and in PROC GENMOD, the Wald F. Because these methods do not produce an equivalent to the ANOVA F² statistic, we identified separate means of reporting effect magnitude, including weighted averages for dependent variables by group or measurement condition and graphical representations of the changes in dependent variables over time.

To minimize the potential for spurious associations resulting from idiosyncratic effects of individual measurement points, all analyses evaluating differences by group or measurement condition except season included months post contact as a covariate, treated as a categorical variable to control for differences without consistent direction across time. The models testing linear changes over time post contact control for season. Age also potentially confounds that analysis. So, where changes over time were evident both by age and months post contact, both predictors were combined into a single model, with sex-by-age or sex-by-months interaction terms if warranted. Other significant predictors from bivariate analysis also were included to rule out confounding. For brevity, only the final model controlling for covariates and including appropriate interaction terms is reported.

EBV values were log transformed before all statistical analyses, but weighted averages are reported as untransformed values to retain intuitive meaning.

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TABLE 2. Nutritional and immunological status for the combined sample and by sex, age, and season

<table>
<thead>
<tr>
<th>BMlz</th>
<th>HAz</th>
<th>HAz ≤ −2</th>
<th>ACz</th>
<th>CRP ≥ 4</th>
<th>CRP ≥ 10</th>
<th>EBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (N = 65)</td>
<td>−0.67 ± 0.83</td>
<td>−3.65 ± 0.84</td>
<td>95.2%</td>
<td>−1.94 ± 0.60</td>
<td>24.7%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Males (n = 47)</td>
<td>−0.68 ± 0.80</td>
<td>−3.70 ± 0.79</td>
<td>99.3%</td>
<td>−2.06 ± 0.59</td>
<td>28.8%</td>
<td>11.0%</td>
</tr>
<tr>
<td>Children/Juveniles (n = 23)</td>
<td>−0.64 ± 0.67</td>
<td>−3.81 ± 0.59</td>
<td>100%</td>
<td>−1.86 ± 0.46</td>
<td>28.3%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Adolescents (n = 30)</td>
<td>−0.73 ± 0.85</td>
<td>−3.64 ± 0.86</td>
<td>98.9%</td>
<td>−2.23* ± 0.60</td>
<td>28.1%</td>
<td>9.4%</td>
</tr>
<tr>
<td>December/January (n = 37)</td>
<td>−0.77 ± 0.84</td>
<td>−3.67 ± 0.86</td>
<td>99.6%</td>
<td>−2.03 ± 0.58</td>
<td>35.1%</td>
<td>8.1%</td>
</tr>
<tr>
<td>June/July (n = 34)</td>
<td>−0.67 ± 0.74</td>
<td>−3.75 ± 0.73*</td>
<td>100%</td>
<td>−2.14** ± 0.61</td>
<td>26.5%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Females (n = 18)</td>
<td>−0.66 ± 0.92</td>
<td>−3.54 ± 0.99</td>
<td>84.3%*</td>
<td>−1.59** ± 0.52</td>
<td>14.0%*</td>
<td>5.9%</td>
</tr>
<tr>
<td>Children/Juveniles (n = 11)</td>
<td>−0.77 ± 0.89</td>
<td>−3.63 ± 0.89</td>
<td>90.0%</td>
<td>−1.71 ± 0.52</td>
<td>7.6%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Adolescents (n = 12)</td>
<td>−0.74 ± 1.07</td>
<td>−3.66 ± 1.16</td>
<td>83.3%</td>
<td>−1.56 ± 0.53</td>
<td>14.0%*</td>
<td>6.1%</td>
</tr>
<tr>
<td>December/January (n = 17)</td>
<td>−0.68 ± 1.02</td>
<td>−3.52 ± 0.98</td>
<td>84.3%</td>
<td>−1.63 ± 0.54</td>
<td>27.5%</td>
<td>10.8%</td>
</tr>
<tr>
<td>June/July (n = 14)</td>
<td>−0.52 ± 0.92</td>
<td>−3.50 ± 1.18</td>
<td>83.3%</td>
<td>−1.46 ± 0.52</td>
<td>3.6%*</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Values displayed in the table are weighted by the number of observations per subject. Subgroup sample sizes indicated on the leftmost column are the number of separate individuals contributing data, not the number of observations, and for some individual measures may be lower due to missing data. Significance levels are for the difference with the most direct comparison group (comparing all females to all males, and comparing age or season within each sex), using restricted maximum likelihood estimation for continuous dependent variables, and generalized estimating equations for dichotomous dependent variables, accounting for repeated (non-independent) measures and controlling for months post contact.

<sub>*P < 0.10, **P < 0.05, ***P < 0.01</sub>

Combining across all ages, no sex differences were evident for BMlz, HAz, CRP ≥ 10, or LogEBV. However, compared to boys, girls were marginally less likely to be stunted ($\chi^2(1) = 2.78, P < 0.10$), and had significantly higher ACz ($F(1, 60) = 7.77, P < 0.01$) and lower prevalence of elevated CRP ($CRP ≥ 4; \chi^2(1) = 3.93, P < 0.05$).

Male children and adolescents did not differ by BMlz, HAz, HAz ≤ −2, CRP ≥ 4, CRP ≥ 10, or LogEBV. Adolescent males had significantly lower ACz ($F(1, 5) = 13.26, P < 0.05$) than did male children. Girls exhibited a marginally higher prevalence of elevated CRP among adolescents than children ($CRP ≥ 4; \chi^2(1) = 3.48, P < 0.10$), but no other significant differences.

Hence, average child nutritional status remained poor for the sample as a whole, and for males and females of every age. In the middle post contact period, females had better growth status (lower stunting) and current nutritional status (higher ACz) than boys on average, and lower average levels of immune system activation as measured by CRP but not EBV.

Sex differences in variation across seasons

All measurements included in these analyses were completed during the months of December and January (wet season), or during the months of June and July (dry season). Among males, HAz was marginally lower ($F(1, 23) = 3.59, P < 0.10$) and ACz significantly lower ($F(1, 21) = 11.03, P < 0.01$) during the dry season (Table 2). Among females, elevated CRP was less prevalent during the dry season (CRP ≥ 4; $\chi^2(1) = 5.47, P < 0.05$). Hence, growth markers were significantly variable by season only in males, but the reverse is true for inflammation.

Changes over time: secular trends by cohort

Secular trends by cohort can be used to tap changes in the status of Hagahai children during the middle post contact period. The narrow span of time covered by these data and the small sample make a secular trend difficult to detect. Nevertheless, a positive secular trend in BMlz, ACz, HAz, or the immune markers could provide evidence for generally improving conditions. The sample was split into tertiles based on estimated birthdates, represented here as months before (negative) or after (positive) December 1983 contact: the first tertile (n = 23) comprises −174 to −113 months; the second (n = 21), −112 to −43 months; the third (n = 21), −42 to +18 months. The observations were stratified by sex and age category (children/juveniles: 5–12.9, adolescents: 13–20 years). This creates 12 cells (3 cohorts X 2 sexes X 2 age groups), each of which includes at least 5 observations, except the absence of children/juveniles in the first cohort (by 60 months post contact), they were all older than 13), and of adolescents in the third cohort (by 103 months post contact, none had reached age 13). The first and second birth cohort were compared using independent samples t-tests for a secular trend in adolescent growth or immunological markers. The second and third cohorts were compared for a secular trend among children/juveniles.

The birth cohorts showed no difference for any outcome among boys or girls for HAz, ACz, LogEBV, stunting, CRP ≥ 4, or CRP ≥ 10. However, in the first cohort for adolescent boys, BMlz $M = −0.47 ± 0.23$, and in the second, $M = −1.07 ± 0.16$, a marginally significant decline ($t(28) = 1.98, P < 0.10$). Moreover, in the second cohort for child/juvenile girls, BMlz $M = −1.33 ± 0.32$, and in the third, $M = −0.21 ± 0.31$, a significant improvement ($t(8) = 2.51, P < 0.05$). These findings suggest a positive secular trend for BMI among younger girls and a negative trend among older boys but also could reflect cohort differences in the accuracy of age determinations.

Changes over time: months post contact

An alternative way to identify change across time is longitudinal analysis using time post contact (60–103 months) as a continuous predictor variable. Stunting, elevated CRP, highly elevated CRP, and LogEBV manifested no significant changes by months post contact after controlling for relevant covariates, so no final models are reported.
In bivariate modeling, ACz declined with time post contact, in males and females ages 5–20, based on restricted maximum likelihood modeling under SAS PROC MIXED. For males, the linear prediction is described by the equation $y = -0.00306x - 3.4338 (P < 0.05)$; and for females, $y = 0.00896x - 4.2637$ (ns). The interaction is significant ($P < 0.01$).

ACz. In bivariate modeling, ACz declined with time post contact overall ($B = -0.004, F(1, 72) = 4.99, P < 0.05$) but declined only in males ($B = -0.010, F(1, 48) = 24.84, P < 0.001$), whereas increasing in females ($B = 0.006, F(1, 23) = 5.55, P < 0.05$). Preliminary analyses revealed no age effect or age X sex interaction after controlling for months post contact and the months X sex interaction. The final model included time post contact and its interaction with sex, with season and birth order as covariates. Season and birth order were neither significant nor was there a main effect of time post contact ($B = 0.006, F(1, 70) = 0.56, ns$). Sex and its interaction with time post contact were significant (sex: $B = 0.834, F(1, 51) = 6.48, P < 0.05$; sex X time post contact: $B = -0.016, F(1, 70) = 24.29, P < 0.001$). The bivariate interaction is illustrated in Figure 3 and reflects a positive slope in females but a negative slope in males.

These models provide no evidence for generally improving nutritional or immunological status between 1988 and 1992. Rather, HAz and ACz of boys declined over time, whereas BMIz and ACz increased among girls, and for all measures, girls had the significantly more positive slope.

Sex ratios

Finally, sex ratios can confirm suggestions that parents are disfavoring daughters. The sex ratio by age for this sample is displayed in Table 3, along with sex ratios from surveys for this same population from 1984 to 1987 (Jenkins, 1988). The statistical significance of the difference between sex ratios in the early and middle periods post contact cannot be established without raw data from 1984 to 1987; however, the male bias appears to have strengthened at all ages.

DISCUSSION

Previous reports concerning Hagahai children presented a grim picture of severe stunting at all ages, wast-
TABLE 3. Sex ratios by time period (males per 100 females)

<table>
<thead>
<tr>
<th>Sample</th>
<th>Sex ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison Sample, 1984–1987, Ages 5–10&lt;sup&gt;a&lt;/sup&gt;</td>
<td>153</td>
</tr>
<tr>
<td>Comparison Sample, 1984–1987, Ages 10–15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>207</td>
</tr>
<tr>
<td>Comparison Sample, 1984–1987, Ages 15–20&lt;sup&gt;a&lt;/sup&gt;</td>
<td>275</td>
</tr>
</tbody>
</table>

<sup>a</sup>1984–1987 sex ratios are from Jenkins (1988). That report does not include exact sex ratios, but displays a population pyramid from which approximate sex ratios for each age range were derived.

The period from which the study data were drawn, 5–9 years post contact, child well-being as marked by BMI, stature, inflammation, and humoral immune activity was neither clearly worsening nor improving for the sample as a whole. Although heavy infectious disease load predated December 1983, Jenkins and coworkers (Jenkins, 1987; Jenkins, 1988; Jenkins et al., 1989) have identified both beneficial and deleterious effects linked to intensive contact, with increased medical assistance offset by new avenues for infectious disease exposure. The overall stability in child nutritional and immunological status suggests that countervailing beneficial and deleterious effects of contact were in balance. Yet belying stability in the combined sample, females showed amelioration of AC and BMI, whereas males moved in the opposite direction with respect to AC and stature. Hence, culture change during the middle post contact period was not experienced equally by sex.

The period of acute phase response, or the humoral immune activation on average was high, whether measured through the acute phase response, or the humoral response to a reactivating Epstein-Barr Virus.

Systematic overestimation of age would exaggerate apparent stunting and poor nutritional status by comparing children and adolescents against an older reference group or older children from other PNG populations. Yet severe stunting and low ACz were not specific to older children or adolescents, and both sexes combined showed no general trend in HAZ or ACz by age. The only age-related trend, lower ACz in older males, is an expectable result of delayed puberty (Woodruff and Duffield, 2002). Hagahai BMI was closer to the reference standard, and wasting rare. However, near-normal weight for height is common in populations experiencing chronic undernutrition and high pathogen load, and not per se indicative of good health (Heywood and Norgan, 1992). Hagahai immune activation on average was high, whether measured through the acute phase response, or the humoral response to a reactivating Epstein-Barr Virus.

In sum, 1988–1992 Hagahai children were on the low end of the height and weight range for this subset of contemporaneous PNG groups: short and light compared to the smaller 1960s and larger 1980s rural Bundi (Eveleth and Tanner, 1990; Ulijaszek, 1990; Zemel and Jenkins, 1989). Hagahai boys and girls were shorter and lighter than Manus and Wopkaimin children (Lourie and Taufa, 1986; Schall, 1991, Uljiaszek, 1990; Zemel and Jenkins, 1989). The Bundi are a geographically proximate group in Madang province with a longer history of contact and of medical, nutritional, and economic modernization, with data available from 1966 to 1967 and from 1983 to 1984, following improvements in child growth status (Zemel and Jenkins, 1989). The more distant Wopkaimin were measured when living as hunter-horticulturalists in the early stages of rapid ecological and cultural change following construction of a major mining complex (Lourie and Taufa, 1986). The Hagahai in the middle post contact period had lower AC than Manus, 1980s Bundi, and Wopkaimin children for both sexes at every age (Eveleth and Tanner, 1990). Hagahai boys and girls were shorter and lighter than Manus and Wopkaimin children (Lourie and Taufa, 1986; Schall, 1991), and at most ages fell between the smaller 1960s and larger 1980s rural Bundi (Eveleth and Tanner, 1990; Uljiaszek, 1990; Zemel and Jenkins, 1989). Hagahai boys and girls also were shorter and lighter than Kaimapit and Karkar coastal populations and Mount Hagen highlanders (Ulijaszek, 1990; AC data not available), and similar to the neighboring Haruai, possibly with minor improvement compared to Hagahai children measured immediately after contact (Jenkins, 1987).

During the period from which the study data were drawn, 5–9 years post contact, child well-being as marked by BMI, stature, inflammation, and humoral immune activity was neither clearly worsening nor improving for the sample as a whole. Although heavy infectious disease load predated December 1983, Jenkins and coworkers (Jenkins, 1987; Jenkins, 1988; Jenkins et al., 1989) have identified both beneficial and deleterious effects linked to intensive contact, with increased medical assistance offset by new avenues for infectious disease exposure. The overall stability in child nutritional and immunological status suggests that countervailing beneficial and deleterious effects of contact were in balance. Yet belying stability in the combined sample, females showed amelioration of AC and BMI, whereas males moved in the opposite direction with respect to AC and stature. Hence, culture change during the middle post contact period was not experienced equally by sex.

Hagahai immunological activation is unusually high

That CRP and EBV are novel markers of child status in the developing world enjoins caution in their interpretation for Hagahai children. Nevertheless, in non-Western populations, elevated CRP at the population level has been associated with a more pathogenic environment, and at the individual or subgroup level reflects differences in the immune response to pathogen exposure (McDade, 2003; McDade et al., 2008). Substantially elevated CRP among 5–10-year-old children, defined as >5 mg/L, was found in 5.8% of Samoans and 6.0% of Rendille pastoralists of Kenya (McDade, 2003)—similar to the prevalence
of extremely high CRP (>10 mg/L) among Hagahai children. Only 12.6% of Bolivian Tsimane’ ages 2–10 had CRP >4 mg/L, despite a highly pathogenic environment (McDade et al., 2008). All groups in the present sample exceeded that prevalence, except females under age 13. Thus, even by the standards of other ecologically challenged populations, the Hagahai resided in a highly pathogenic environment.

Exceptionally high EBV antibody levels also prevailed in this sample. We are aware of no previous report, wherein average values among children or adults approach 190 A.U. with the DiaSorin anti-EBV VCA assay kit, as seen among the Hagahai. McDade et al. (2000) reported mean EBV 95.3 A.U., SD 65.8 among Samoan children ages 4–20. Worthman and Panter-Brick (2008), working with ecologically challenged Nepali boys 10–14 years of age, reported mean EBV 77.7 A.U., or 74.7 for nutritionally stressed homeless street children (mean HAz – 2.82). Moreover, the Hagahai were unusual in that EBV antibodies were equally elevated regardless of sex, age, and season, and had no association with nutritional status or inflammation.

Worthman and Panter-Brick (2008) have suggested that under conditions of childhood adversity, the energetic costs of mounting a humoral response become significant and only those who are relatively healthy have high EBV titers. The present findings call that interpretation into question. Among the Hagahai, EBV titers may be secondary to high infectious disease load. Total IgG and IgM levels among Hagahai in the mid 1980s were higher than any contemporaneous population in Papua New Guinea, due in part to malaria and consequently high prevalence of Hyper-reactive Malarial Splenomegaly (HMS) (Jenkins et al., 1989). Under such conditions the immune system’s compromised state would loosen constraints on EBV reactivation. Moreover, increased immune surveillance may result from repeated infections in children living under the poorest conditions (Ulijaszek, 2000). Thus, although EBV antibody levels among Hagahai children are consistent with pervasive immunological stress, further research in ecologically challenged populations will be required to clarify what variation in EBV titers signifies under such conditions.

Surviving females are canalized

While the overall health profile of Hagahai children from 1988 to 1992 was characterized by continuing high infectious disease load and slow growth, both parent and child factors may influence the extent to which the deleterious and salutary correlates of culture change differentially impinge upon boys’ and girls’ development. Table 4 reviews predictions from the two major hypotheses regarding differential impact by sex, and how well each was supported.

Girls were less likely to be stunted and had higher ACz on average. The only secular trends evident in either sex were an increase in BMIz among girls and decrease among boys from 1988 to 1992, and there was a growing gap between the sexes in mean nutritional status, as females had a more positive slope than males for BMIz, HAZ, and ACz across time post contact. Yet, the sex ratio from 1988 to 1992 was more male-biased than previously reported at every age from 5 to 20 (cf. Jenkins, 1988). Hence, the sex discrepancy in nutritional status did not likely reflect daughter preference, particularly given ethnographic reports and infant health data suggesting exacerbation of male preference from 1984 through 1992 (Worthman et al., 1993).

If male–female differences in nutritional status were not driven by parental preference toward females, then the sexes must have differed in their response to adversity. The better overall nutritional status of females than males relative to the U.S. reference populations was predicted if females are canalized. Females also showed no significant fluctuations in nutritional status by season, whereas males varied seasonally in both ACz and HAz, although the smaller female sample size makes it difficult to draw unambiguous conclusions from this finding.

Human females’ life history strategy is influenced by their limited reproductive lifespan and the requirement for high energetic investment in offspring (Bogin, 2001; Walker et al., 2006). Infants whose mothers are short in stature or have low energy reserves are more likely to have experienced intrauterine growth restriction (Kramer et al., 2000), which in turn predicts higher mortality, morbidity and cognitive deficits during the perinatal period and later in life (Pallotto and Kilbride, 2006). Prereproductive female growth, therefore, represents an investment in future reproduction and the condition of future offspring. Although children living under high extrinsic mortality risk should accelerate maturation (Walker et al., 2006), canalized female growth patterns among ecologically challenged human populations may reflect the imperative to establish as rapidly as possible the energetic resources required to successfully reproduce at all.

Human females benefit from pooling of energy through coordinated social behavior and juvenile provisioning, which permits greater simultaneous investment in maintenance and growth under challenging ecological conditions than can be achieved in other mammalian species (Kramer et al., 2009). However, disfavored Hagahai females did not appear to receive the degree of buffering through juvenile provisioning described among many other populations. Hence, among Hagahai girls, a strategy of canalization should have elevated intrinsic mortality risk by diverting resources from maintenance toward growth even while increasing long term maintenance costs (McDade et al., 2008; Walker et al., 2006). Although

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Predictions</th>
<th>Supported?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Canalization</td>
<td>Better nutritional/growth status among girls than boys</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Lower immune activation among girls than boys</td>
<td>Partial (CRP only)</td>
</tr>
<tr>
<td>Survivorship Effects</td>
<td>Better nutritional/growth status among girls than boys</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Average condition of female children/adolescents appears better as conditions worsen for female infants</td>
<td>Yes (Mean female condition improves as sex ratios become more male-biased)</td>
</tr>
</tbody>
</table>

*Where culture change involves increases in trade, wage labor, pathogen load, and stationary settlement; and, where ongoing changes 5–9 years post contact occur against the backdrop of conditions inherited from the early post contact period, including high infant mortality, a male-biased sex ratio, and poor general adult and child health.
The statistical analysis appropriately account for the variability of the serum samples. It is unlikely that, in the context of follow-up for some of the children, and the potential for phenotypic correlation can only be resolved using prospective analysis not permitted by the current data. In sum, immunological data provide equivocal support for a life history strategy of canalization among females.

Our final consideration concerns the role of differential survivorship. Where IMRs exceed 50% and disproportionately affect females, girls with atypically high resilience to adversity are overrepresented among survivors. Physiologically based vulnerability or resilience in infancy may persist later in life. For example, low birthweight is associated with higher infant mortality and lower stature through childhood and adolescence despite catch-up growth (Martorell et al., 1998; Victora et al., 2001). Birthweights are not available for the Hagahai because nearly the entire sample was born before a permanent aid station or regular patrols were established. Yet, disproportionately strong selection for infant resiliency among Hagahai females would yield a surviving female population more refractory to adverse effects on average than males to the effects of continuing adversity: as is seen here, females will appear canalized or buffered. The finding that boys' nutritional status relative to U.S. reference standards was still declining during the middle post contact period while girls mostly improved, even as female infants' health declined relative to males, provides further support for the existence of a survivorship effect. Improvements in population-level nutritional status among girls ironically may reflect an intensification of selection for resilient survivors. Moreover, variation in the treatment of females is expected in any population. Schepers-Hughes (1985) demonstrated that high infant mortality in a Brazilian shantytown was associated with maternal emotional detachment and selective neglect toward infants seen as too weak to survive, in contrast to those perceived as "fighters." By analogy, it is possible that surviving females not only were constitutionally more resilient but also were favored by parents relative to other females who did not survive. In that case, physiologically and behaviorally mediated survivorship effects operate synergistically to create the appearance of female canalization.

**Limitations**

This analysis is limited by the small sample size, the inconsistency of follow-up for some of the children, and possibly the age of the serum samples. It is unlikely that, based on size alone, this sample substantially misrepresents the population from which it was drawn given that the population also is very small and nearly all children were measured at least once. The mixed models used in the statistical analysis appropriately account for the varying number of observations per individual. The inconsistent inclusion of some participants during follow-up, however, is still a source of concern. We cannot exclude confounding due to differences between those who remained in the sample and those who did not. Apparent changes in nutritional or immunological outcomes with time could be an artifact of change in the composition of the sample. This was unavoidable and reflects the scattered and mobile nature of the population in an extremely remote part of Papua New Guinea. Nevertheless, restricted analyses using only participants present at 103 months do not change our findings.

**CONCLUSIONS**

Despite the limitations, these data present a unique record of physiological correlates of rapid culture change shortly following contact. We draw several conclusions with implications for future work within ecologically challenged populations on the economic margins of the developing world. As expected, Hagahai outcomes on the whole were poor. Also as predicted, the physical impact of culture change on girls and boys was not commensurate, even where adversity was nearly universal. Every component of the present analysis reveals sex differences: different average nutritional and immunological status; differences in seasonal variability; differences in changes with time post contact; and biased sex ratios. The pattern accords with existing literature concerning the Hagahai. But only when canalization and survivorship effects are considered can conditions that apparently increasingly favored males be reconciled with better nutritional status among girls.

The findings generally support predictions from a female canalization model. Females were less likely to be stunted, had greater AC for their age, and showed lower activation of the acute phase response. This accords with a life history strategy that emphasizes growth over maintenance toward realizing future reproductive potential. The picture is complicated by survivorship effects. Where infant mortality is high, children surviving to age 5 are those whose microecologies and constitutions allowed them to withstand a strong early selection regime. Selective survivorship may lead to population growth and disease patterns distinct from what would be evident were survivors truly a random sample of those who are born into the population. The gendered microecologies prevailing among Hagahai during the middle years post contact systematically subjected boys and girls to different levels of early selection pressure. This study suggests that differential selection for resiliency can exaggerate female canalization, yielding an apparent advantage for girls that actually reflects the consequences of disadvantage.

**ACKNOWLEDGMENTS**

This report honors the memory of Carol Jenkins, the visionary medical anthropologist who, during her tenure at the Papua New Guinea Institute for Medical Research, designed and implemented the research from which the analyses in this report are drawn. The authors thank the Hagahai who participated in the years of study over the postcontact period; the staff of PNG IMR who collected the sera and measures; and James Bindon and others.
Christopher Lynn for feedback on an earlier version of this manuscript.

LITERATURE CITED


