LIFE HISTORY TRADE-OFFS IN GROWTH AND IMMUNE FUNCTION: THE BEHAVIORAL AND IMMUNOLOGICAL ECOLOGY OF THE SHUAR OF AMAZONIAN ECUADOR, AN INDIGENOUS POPULATION IN THE MIDST OF RAPID ECONOMIC AND ECOLOGICAL CHANGE

by

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Life history theory examines the allocation of resources among competing demands, including growth, immune function, and reproduction. Immune function can itself be divided into innate, cell mediated, and humoral responses. For humans, factors like economic condition, disease exposure, and social milieu are all hypothesized to affect life history allocations. For the Shuar of Amazonian Ecuador these factors are rapidly changing as traditional subsistence hunting and horticulture give way to wage labor and Western medicine.

This dissertation presents fieldwork conducted amongst the Shuar between 2005 and 2009. It is among the first studies to test for life history trade-offs between different branches of immunity and growth across market conditions. Shuar data include anthropometrics (n=1,547), biomarkers (n=163), and household compositions (n=292).

Comparison samples include the Shiwiar of Ecuador (n=42), non-indigenous Ecuadorian *colono* children (n=570), the Tsimane of Bolivia (n=329), and the 2005-2006 U.S. NHANES (n=8,336).

The dissertation finds significant differences between both populations and Shuar villages in growth and immunity. Increasing market integration is associated with poorer growth, but household factors mediate these changes. Adult males have positive effects on child growth in acculturated areas with wage labor and in distant areas where fishing and hunting remain important but not in intermediate areas. Children have consistent negative effects on one another's growth, suggesting competition for resources. Poorer growth is also associated with higher levels of immunoglobulin E (IgE), a humoral response to helminths. In contrast, C-reactive protein, an inflammatory marker, has a positive association with growth. This divergence between humoral and innate immunity is consistent with a lasting reallocation of immune resources towards a T_H2 response in helminth infected individuals. The age-profile of IgE also varies across market conditions: comparing the Shuar with samples from the U.S. and Bolivia, the age of peak IgE is correlated with the level of peak IgE in each population, providing some of the first evidence for a "peak shift" in immune response. Overall, these results support the hypothesis that local conditions lead to the adaptive "tuning" of trade-offs between branches of immunity and growth.

This dissertation includes previously published and unpublished co-authored material.

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Dedicated to Charles Darwin, who said,

"I am turned into a sort of machine for observing facts and grinding out conclusions."

I know how you feel, Chuck.

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CHAPTER I

INTRODUCTION

LIFE HISTORY THEORY

Humans, like all organisms, face trade-offs when allocating energy and other resources between competing demands. For instance, energy can be used to increase height, or muscle. It can be stored as adipose tissue for future use. It can be invested in mate acquisition or offspring production. Or, it can be used to strengthen immune defenses, protecting against pathogens and other insults. Energy can be used for any of these things. However energy used in one way becomes unavailable for other uses. As are all things, living organisms are bound by the law of conservation of energy. Organisms are limited by the energy available to them, and must budget energy effectively to be successful. Those who do this well survive, reproduce, and pass their genes on to future generations. Over time, genes contributing to optimal energy allocation are selected for and become more common.

In biological systems, the first law of thermodynamics has been restated as life history theory. Life history theory addresses the tradeoffs organisms face and the solutions natural selection evolves to address them (Alexander, 1974; Charnov & Schaffer, 1973; Charnov, 1991; Charnov, 1993; Hill & Hurtado, 1996; Hill & Kaplan, 1999; Kaplan *et al.*, 2000; Lessels, 1991; MacArthur & Wilson, 1967; Schaffer, 1974;

Stearns, 1976; Stearns, 1992). Typically, when discussing life history allocations, resources are divided into broad categories, such as growth, somatic maintenance, and reproduction. The optimal allocation between these competing categories is different for each organism, and depends not only on relatively static factors that affect all organisms of the same species or population, but also upon dynamic factors that change throughout the lifespan. As a consequence, life history allocations change as an organism progresses through life stages or moves to a new environment. Since time is such an important factor in life history allocations, life history tradeoffs can be phrased either in terms of instantaneous allocation between demands such as growth and reproduction, or more generally in terms of lifetime allocations between demands such as past and future reproduction, quantity versus quality of offspring, and direct versus indirect reproductive effort.

Life history theory actually gets its name from the fact that tradeoffs are related to the timing of life events. Key features of an organism's life history include the length of the juvenile period, the age of first reproduction, the spacing of births, and the timing of menopause. Each of these represents a significant reallocation of energy. For example, organisms such as mammals have determinate growth that ends once adult size is reached (Bogin, 1999). The end of the juvenile period often correlates with the age of first reproduction, because it is at this point that a significant reallocation of energy occurs, away from growth and towards reproduction. Similarly, menopause represents a cessation of direct reproductive effect. Many think that the cessation of reproductive effort at menopause is because grandmothers can more efficiently use their available

energy by investing in existing offspring or other kin, such as grandchildren (Hawkes *et al.,* 1997; Hawkes *et al.*, 1998; Williams, 1957), although this is debated (Mace and Sear, 2005).

Menopause occurs in very few non-human animals, and is just one of the features that makes human life histories unique. Compared to other organisms, the human life history is characterized by long lifespan, an extended juvenile period, delayed age of first reproduction, transfers of resources between individuals, and unprecedented investment into mental capacities (Bogin, 1999; Kaplan *et al.*, 2000). The challenge for much evolutionary anthropology is to understand how these unique features evolved and how humans adjust their life histories to match the environments they find themselves in.

Parental Investment Theory

Parental investment theory is an aspect of life history theory that focuses on tradeoffs that parents face between investing in different offspring (Trivers, 1972). Parental investment is a theoretical concept and is essentially any resource, be it material or immaterial (such as time or knowledge) that given to one offspring cannot be given to another. Parents are expected to vary their investment into offspring based on a number of criteria, including the condition of offspring, the relative benefit each offspring will receive from investment, and other potential uses for the investment. For males, paternity may be uncertain, so males are also expected to vary their investment based on their certainty of paternity. Put into more general terms, we can say that parents are expected

to invest based on the likelihood that a given offspring will be able to translate investment into future parental fitness.

One of the most fundamental trade-offs parents face has to do with the number of offspring to produce. Since the number of offspring a parent has determines the fraction of investment that goes to each, parents can produce many offspring and invest very little in each, or produce few and invest heavily (Clutton-Brock, 1991; Lack, 1947). This is referred to as the "quantity-quality trade-off" (QQ). The QQ trade-off is closely linked to other fundamental life history questions. For example, the spacing of births is essentially a QQ problem. Individuals that space their births more widely are able to invest more in each offspring before beginning investment in another. However, these organisms risk producing fewer total offspring due to their slower rate of reproduction. The trade-off between present and future reproduction is similarly connected. Organisms must choose whether to hoard their resources (usually in the form of fat stores, body size, and so on) in order to produce high quality offspring in the future, or spend their resources now in order to produce offspring quickly. Many factors affect the solutions to these problems. One factor is mortality risk. If there is a good chance you will die tomorrow, then it is better to spend your resources today rather than risk dying with nothing (e.g. Polak 1998).

Organisms may also face a trade-off between direct parental investment and indirect investment into kin. In humans this is especially pronounced, since humans live in complex social groups and engage in extensive resource transfers between both related and unrelated individuals (Gurven 2004). Some argue that humans are best thought of as

cooperative breeders, as exemplified by the adage "it takes a village to raise a child" (e.g. Hrdy 2009). In humans, adolescents, grandparents, and even unrelated individuals may all share investment in a single child (Mace and Sear 2005). Humans may even adopt unrelated children. Human life histories likely reflect this cooperation, and analyses of parental investment in humans must take indirect investment into consideration.

Ecological Immunology

In addition to broad categories like growth, reproduction, and somatic maintenance, life history trade-offs can be examined at a much finer level of detail (Figure 1.1). Of particular interest for this dissertation are trade-offs between aspects of immune function. The immune system is multi-faceted and trade-offs exist between non-specific defenses such as inflammation, cell-mediated defenses such as cytotoxic T-cells, and humoral defenses based on the circulation of antibodies (Janeway, 2005; McDade & Worthman, 1999; McDade, 2003; Sheldon & Verhulst, 1996).

The body is expected to regulate immune function carefully because responding to disease is *costly.* Fever, for example, is estimated to increase metabolic rate by 13% for every degree increase in body temperature, while sepsis or systemic infection can increase metabolic costs by 50% (Lochmiller & Deerenberg, 2000). Protein synthesis increases during an immune response, from about 3.5g to 6g of protein per day per kilogram of body weight, an estimated expense of 285 kcal/day (McDade, 2003). This increase in protein synthesis requires not just energy, but amino acids sometimes only obtainable from dietary protein. Specific types of immune defense are also regulated by

nutrient availability; for example, Vitamin A seems to increase the response of helper T-cells known as T_H1 cells (Long & Nanthakumar, 2004). Across species, mounting an immune response decreases growth, survival, and reproduction (Klein & Nelson, 1999; Sheldon & Verhulst, 1996; Uller *et al.*, 2006). For example, in humans periods of illness during childhood can result in growth delay and stunting (Bogin, 1999; McDade *et al.*, 2008; Victora, 1992).

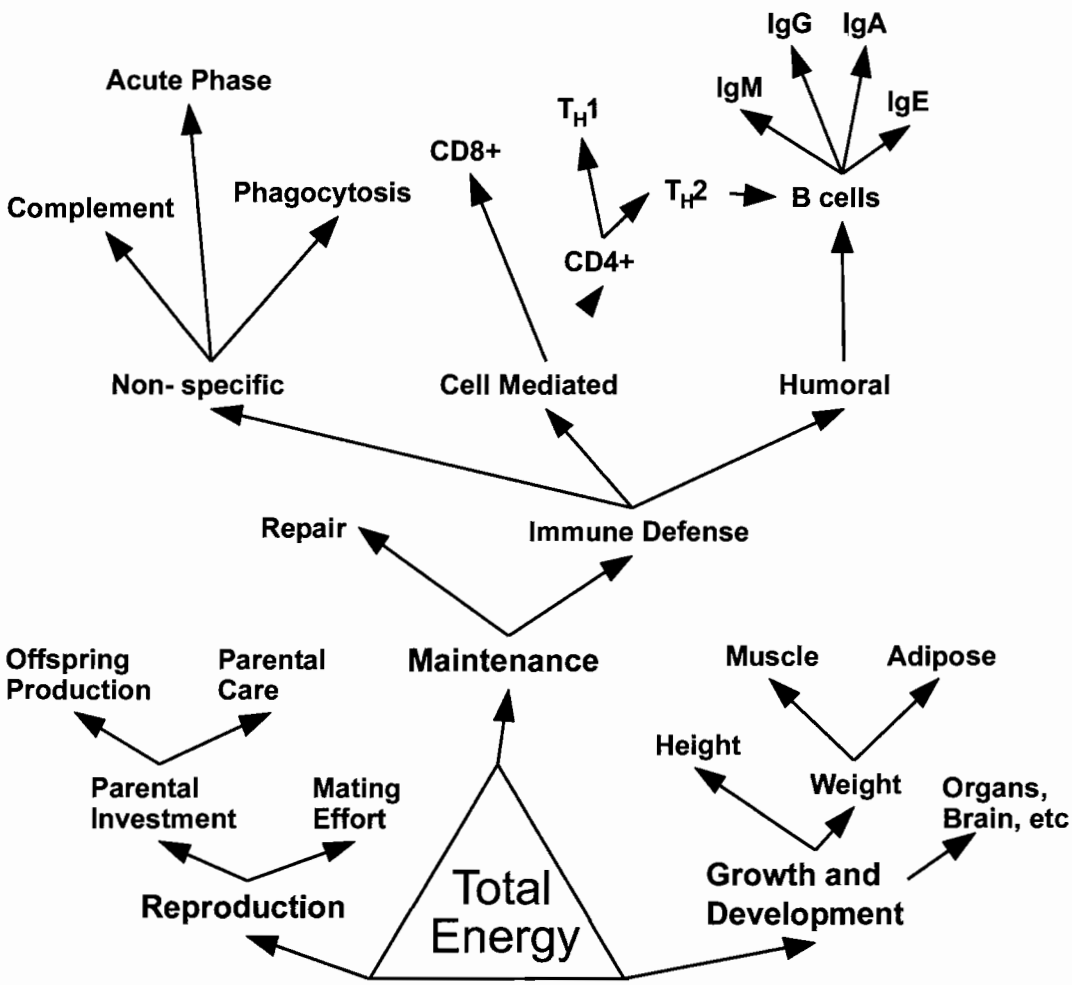

Figure 1.1. Simplified schematic of hypothesized life history tradeoffs

Each of the several different types of immune defense has its own energetic costs and benefits. Although the mechanistic and functional organization of trade-offs is only partially understood, immune responses can be grouped categorically into innate (non-specific) immunity, cell-mediated immunity, and humoral immunity. Non-specific defenses are generic defenses (such as fever) that do not need to be acquired over the lifetime. Cell mediated defenses depend on phagocytic cells to attack invading pathogens. Humoral defense involve the circulation of antibody within the blood stream that can bind to and detect pathogens. Energy must be allocated between these immunological pathways at all levels of this hierarchy (Campbell *et al.,* 2003; Long & Nanthakumar, 2004; McDade, 2003; McDade, 2005).

The study of how immune function responds to ecological and social variables is referred to as *ecological immunology* (McDade & Worthman, 1999; McDade, 2003; Sheldon & Verhulst, 1996). Variables studied in ecological immunology reflect not just environmental demands (e.g., defending against helminths vs. defending against viral infections) but also what might be thought of as *immune strategies*. In addition to energetic costs, each type of immune response has other unique costs and benefits. For example, inflammation is a non-specific immune defense that will help clear a pathogen. But inflammation is more likely to cause collateral damage, due to oxidative stress, and more likely to increase the long-term risk of chronic diseases such as atherosclerosis and cardiovascular disease than are cell-mediated or humoral immunity (Pearson *et al.*, 2003; Ridker *et al.*, 1998).

Different immune responses also have different time costs. If an organism has low energy stores or high extrinsic mortality risk, prolonged inactivity and illness can limit mating opportunities or result in fatal energy shortages. Thus defenses which can quickly clear a pathogen, such as inflammation, may be preferred. In longer living organisms with low mortality risk and sufficient energy stores for prolonged immune activation, defenses that limit collateral damage may be preferred, even if they take longer to achieve pathogen clearance (Martin *et al.*, 2008). For these organisms, investing in the future may take precedence over investing in the present.

Life History Theory and This Dissertation

This dissertation presents the results of fieldwork conducted amongst an indigenous Amazonian population of southeast Ecuador, known as the Shuar. The work contained herein was conducted between 2005 and 2009. This study tests a number of predictions derived from life history theory. Chapter II discusses investment into growth, and in particular height, as a life history strategy. In Chapter III, trade-offs in parental investment are meshed with cooperative breeding models to examine the impact of family composition on growth. Chapter IV examines the development of immune function and the relative allocation given to humoral immune responses in three populations. Finally, Chapter V is among the first studies to test for life history trade-offs between different aspects of immunity and growth in a population living across a range of economic and ecological conditions. Although these chapters test for particular trade-

offs independently, it is important to emphasize that life history theory is broad and integrative, and that trade-offs interact on multiple levels.

THE SHUAR OF ECUADOR

The Shuar are an Amerindian group indigenous to the southeastern part of Ecuador. In total, Shuar number over 40,000 (Rubenstein, 2001). As part of the Jivaroan language group, Shuar are linguistically and culturally very similar to groups such as the Shiwiar (Sugiyama & Chacon, 2000; Sugiyama, 2004) and Achuar (Descola, 1994; Descola, 1996). Until recently Shuar were referred to as the Jivaro (or Jibaro) by Spaniards and foreign researchers (Harner, 1984). However, the term Jivaro is considered derogatory, so is preferably not used today. Since the 1800s, Shuar have lived in scattered households across the Upano River Valley, between the eastern Andean foothills and the Cutucu range (Karsten, 1935). Early in the 20th century, introduction of firearms allowed them to expand eastward across the Cutucu into the territory of the neighboring Achuar, so that Shuar now live on both sides of the Cutucu, and throughout the Upano River Valley (Figure 1.2) from the Peruvian border past the Rio Pastaza and north across the Rio Napo.

Shuar are distinctive among indigenous American groups in that they are one of the few groups to have never been conquered. Even before Spanish colonization of Ecuador, Shuar successfully fought off conquest attempts by the Incas. When the Spanish came they too were resisted. Today, Shuar retain a considerable degree of autonomy, and have their own organizations for managing Shuar affairs (Rubenstein,

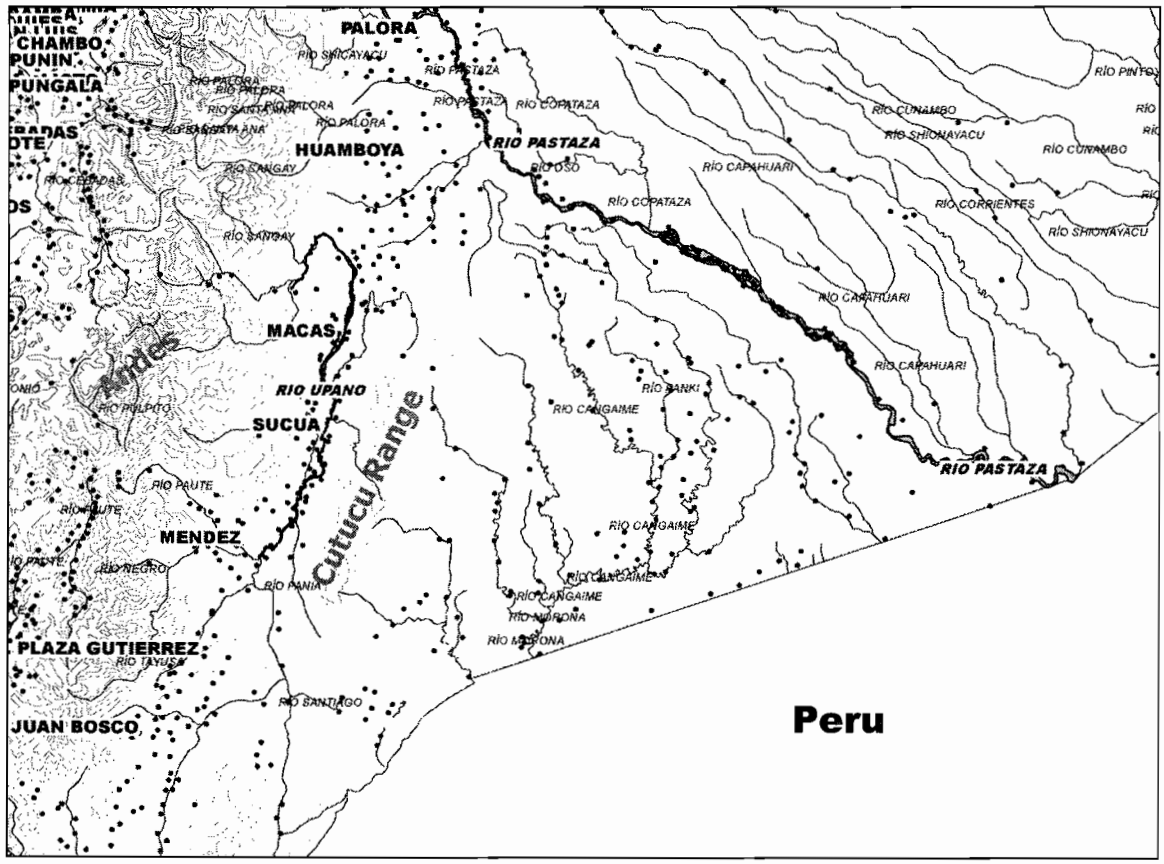

Figure 1.2. Map of Morona Santiago showing the Rio Upano, Rio Pastaza, and Cutucu Range. Points are villages (mostly Shuar, except for those located in the Andes). The map is based on data from the *Sistema Integrado de Indicadores Sociales del Ecuador* released by the *Secretaría Técnica del Frente Social* of Ecuador. See Figure 2.1 for a map of all of Ecuador.

2001). These include the *Federación Interprovincial de Centros Shuar* (FICSH) the *Federación Interprovincial de Nacionalidad Achuar* (FINAE) and the *Federación Independiente del Pueblo Shuar del Ecuador* (FIPSE).

Traditional Shuar subsistence consists of hunting, gathering, fishing, and small-scale swidden horticulture (Descola, 1994; Descola, 1996). Staple foods consist primarily of plantains (Figure 1.3) and sweet manioc, which are frequently boiled. Manioc is cooked,

chewed by women, and fermented to make *nihamanch* (referred to more generally by the Quichua term, *chicha*), which is mildly alcoholic and consumed daily by many Shuar (although to a lesser degree than by the Achuar or Shiwiar). *Chicha* contains a significant amount of plant fiber, making it somewhat more like gruel than a beverage. When meat is brought in by men it is typically roasted or boiled. Other common traditional foods include manioc leaves, papaya, bananas, palm grubs, and fish (Figure 1.4). Today, many Shuar continue to eat these foods, but in many areas hunting is depleted, so chicken serves as a source of protein. Depending on the degree of market integration (see below), many other market foods may also supplement or supplant these traditional aliments.

Figure 1.3. Plantains and bananas are staple foods. Photo credit Blackwell, 2009

Gender roles with regard to subsistence follow a general Amazonian pattern in which females work the garden and gather in the forest, whereas men go hunting or engage in market activities like cutting lumber for sale or raising cattle (e.g. Chagnon 1996; Descola, 1996; Robarchek and Robarchek, 1998). However, these roles are not particularly rigid; men help in the garden and women may accompany men on hunting trips. In general, Shuar culture is highly individualistic and unlike other groups, Shuar

Figure 1.4. Typical foods include palm grubs, manioc, and fish wrapped in a banana leaf and steamed. Photo credit Blackwell, 2009

households rarely share meat. Men hunt in small groups and most of what they obtain goes to the families of those on the hunt.

Market Integration

Although many Shuar continue to subsist by hunting, gathering, and horticulture, lifeways are changing rapidly. According to the 2005 FISCH-FIPSE-FINAE Diagnostic survey (see Chapter III: Data Sources), across Shuar territory thirty-eight percent now own or raise cattle. Cattle are raised for sale rather than private consumption (Figure 1.5). Nineteen percent have sold tress in the past year. Thirty percent grow vegetables for sale. Shuar have emigrated to many other parts of the country and to other countries, such as the United States (Jokisch & McSweeney, 2006; McSweeney & Jokisch, 2007). Some have moved north into areas traditionally occupied by other groups such as the Waorani.

Figure 1.5. Many Shuar now raise cattle on land that has been cleared of native forests. Photo credit Blackwell, 2009

In these areas, Shuar are among the most acculturated indigenous groups (Lu, 2007).

In the past ten years roads have been extended to many Shuar villages in the Upano Valley. Electricity is quickly spreading, so that many Shuar within the Upano River Valley now have access electrical lighting. Across the Cutucu range most Shuar villages still lack electricity, although a few individuals own generators.

Many Shuar villages have primary schools which are attended by almost all young Shuar (Figure 1.6). Relatively few have attended secondary school but the numbers are increasing—about 11% of females and 31% of males age 25 to 34. Most schooling is in Spanish, and as a consequence Spanish is becoming spoken with increasing frequency. Out of 1,760 households surveyed across Shuar and Achuar territory in 2005, 52% spoke only Shuar, 28% both Shuar and Spanish, and 20% only Spanish (Jokisch & McSweeney, 2006). It is likely that if the children were surveyed the percentage speaking only Spanish would be considerably higher.

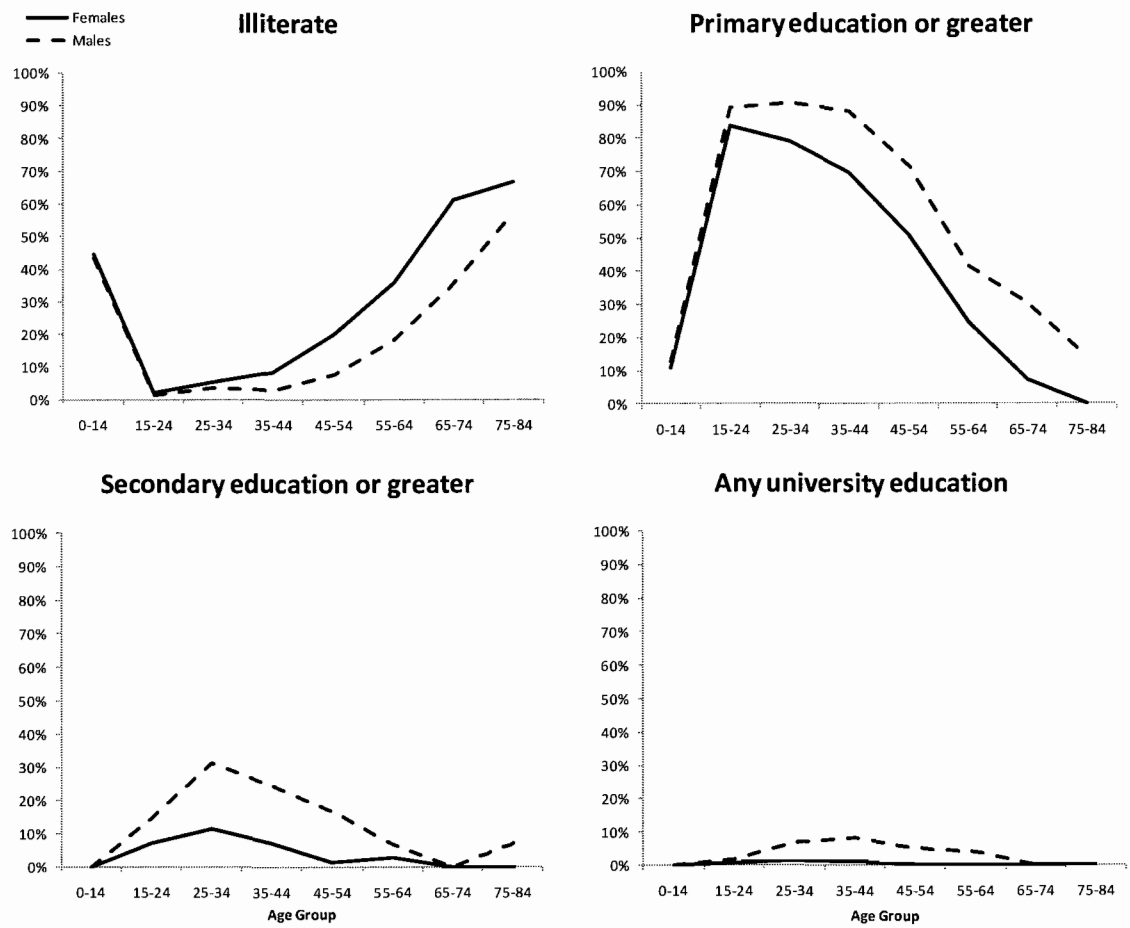

Figure 1.6. Shuar education levels by age group (n=11,907). Data from the FISCH-FIPSE-FINAE Diagnostic of Shuar and Achuar Health Services and Situations. See Chapter III: Data Sources for more information.

Despite these numbers it is important to note that market integration is not occurring uniformly across Shuar territory. Close to the main road running the length of the Upano Valley Shuar may be very acculturated. In towns such as Sucúa, Shuar may be nurses and have children who attend high school and have cell phones, email, and quinceañeras. Across the Cutucu range things are very different. Most food still comes

Figure 1.7. Traditional Shuar houses on the eastern side of the Cutucu mountain range. Photo credit Blackwell, 2009

from hunting, fishing, and gardening, houses are more likely to be traditional (Figure 1.7), and Spanish is spoken by fewer people.

Shuar are actively engaged in these changes. While many desire electricity, Western goods, and so on, many also lament the loss of traditional ways, particularly with regard to the loss of the lands and forest they depend upon. For example, a popular song sung in Shuar goes as follows:

Desde la Montaña (Spanish translation from the original Shuar)

Desde la montaña vengo yo a cantarles a todos ustedes . . .

Para irse a otro pais venden sus fincas, selva y árboles . . .

Abandonan a sus esposas e hijos, y les hacen sufrir.

Shuar, Zaporo, Kichua, Achuar, Andoas, Waorani, Shiwiar

Todos defendamos nuestra selva . . .

From the Mountain (author's translation from the Spanish)

I come from the mountain to sing to you all . . .

To go to another country, sell your farms, forest, and trees . . .

Abandon your wives and children, and make them suffer.

Shuar, Zaporo, Kichua, Achuar, Andoas, Waorani, Shiwiar

We will all defend our forest . . .

Somewhat ironically, there is now a music video for this song, with copies owned by the same Shuar who are cutting down and selling trees to buy televisions and DVD players. The question of market integration is clearly a complex one. However, what is clear is that it should not be thought of only as penetration by an external market, since many Shuar are active participants seeking what they see as new opportunities.

Demography

The Shuar population is growing at an incredibly rapid rate, as is evidenced by the population pyramid in Figure 1.8. Fifty-three percent of Shuar are under age fifteen. For comparison, 28% are under fifteen for the entire world, 30% for Latin America as a whole, and 41% for Africa as a whole (Jokisch & McSweeney, 2006).

The rapid population growth is due to a least three factors. First, Shuar age of first birth is quite young. In a sample from one of the villages we worked in, the median age of first birth was seventeen (Figure 1.9). Second, except for some Shuar in cities,

such as Sucúa and Macas, Shuar are a natural fertility population with fairly short interbirth intervals. We conducted reproductive interviews in a village 45 minutes from Sucúa and found that none of the women interviewed had ever used any form of birth control (or "family planning"). However, this is not due to lack of interest: during interviews many people expressed a desire to learn about family planning. However, most helath promoters are not authorized to dispense birth control and there are logistic and social barriers preventing widespread use. As a consequence, lifetime completed fertility for Shuar is about eight to ten live births per female (Figure 1.10). The final factor leading to population growth is medical care, discussed below.

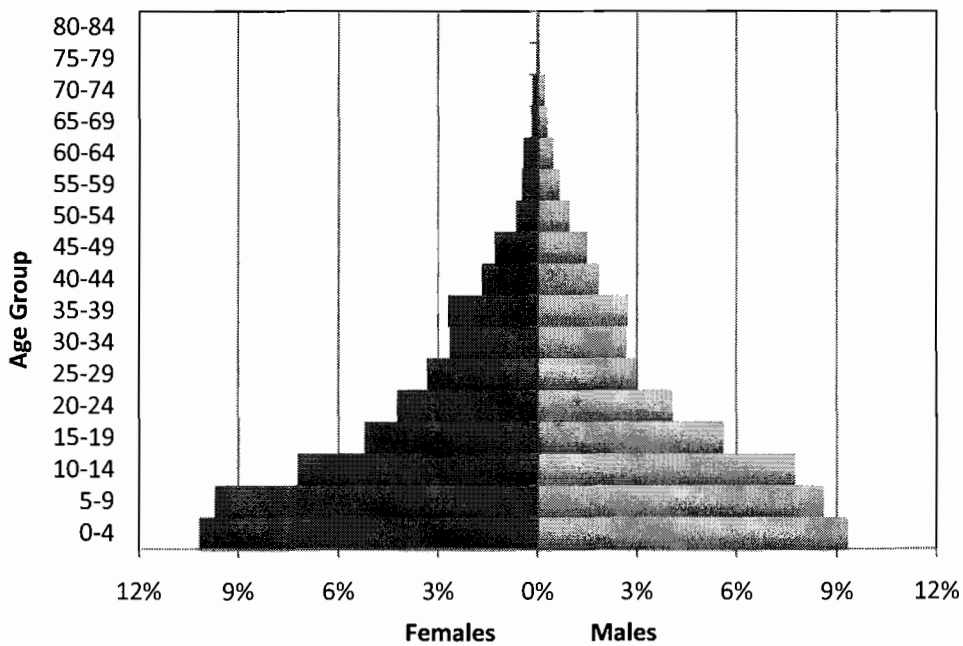

Figure 1.8. Shuar population pyramid (n=11,924). Data from the FISCH-FIPSE-FINAE Diagnostic of Shuar and Achuar Health Services and Situations. See Chapter III: Data Sources for more information.

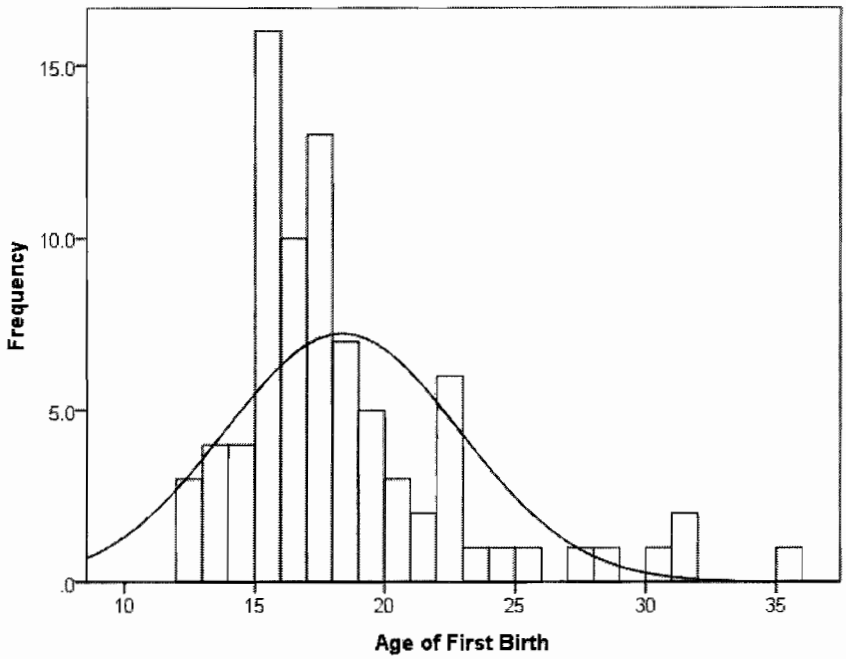

Figure 1.9. Distribution of Shuar age at first birth for a village with an intermediate degree of acculturation. Mean=18.4, S.D. +/- 4.2, Median = 17.2, N=82

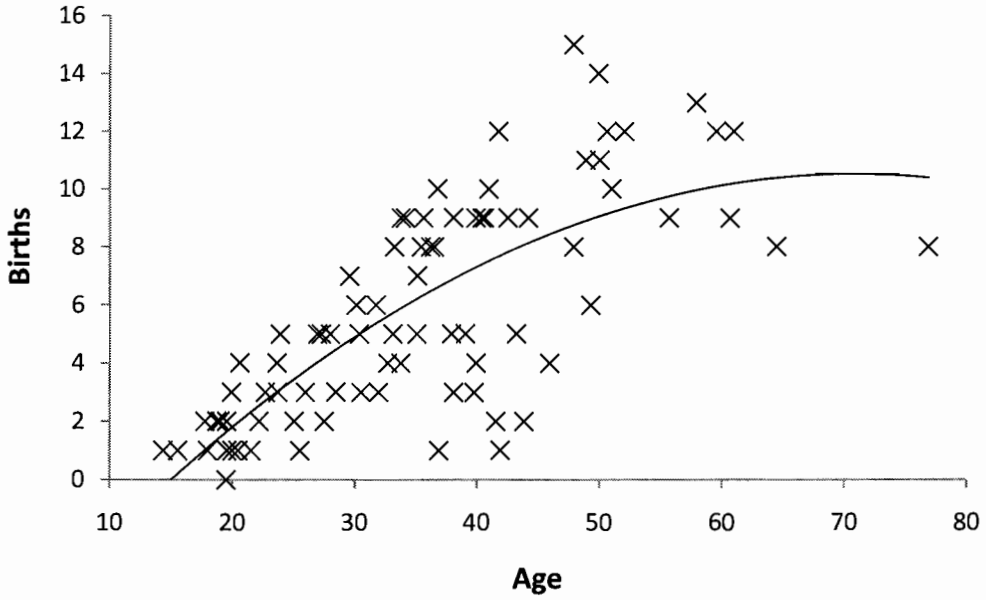

Figure 1.10. Live births by age at interview for a village with an intermediate degree of acculturation (n=82). See Chapters IV and V for info on this village.

Health Care

Shuar have a well developed system of indigenous medicine, which includes the use of medicinal plants (Bennett *et al.,* 2002; Caravaca Cano, n.d) and shamanic curing (Harner, 1984). Many illnesses are attributed to sorcery by enemy shamans who send magical darts (*tsentsak*) which imbed themselves in the victim. Shamanic cures may involve non-biomedical interventions like "sucking" the *tsentsak* from the patient or blowing tobacco smoke. A number of hallucinogens are prepared and used by Shuar (Bennett, 1992). In our experience these are used by many Shuar, not only shamans. Although the use might be considered recreational, it is also spiritual for most Shuar, who believe the use of drugs such as ayahuasca can give visions of the future, glimpses of spirits, and reveal pathways their lives will follow or power they have (Mader and Gomez, 1999).

In the last five to ten years the *Ministerio de Salud Publico de Ecuador* has set up health clinics in many of the larger Shuar villages (Figure 1.11). Most of these are rudimentary and staffed by local health promoters, usually Shuar with very basic medical training. A smaller number of villages also have doctors or nurses; even more have *uwishin* (shaman). Although Western medicine is becoming much more prevalent, many Shuar still prefer to see *uwishin* for many ailments, or will seek out *uwishin* when western remedies fail (Figure 1.12). Reported recovery rates are similar for uwishin and western treatments (Figure 1.13).

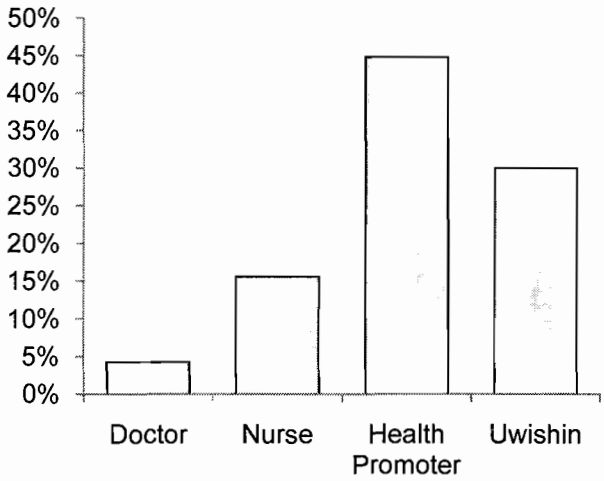

Figure 1.11. Percentage of Shuar villages with health personnel (n=257). Data from the FISCH-FIPSE-FINAE Diagnostic of Shuar and Achuar Health Services and Situations. See Chapter III: Data Sources for more information.

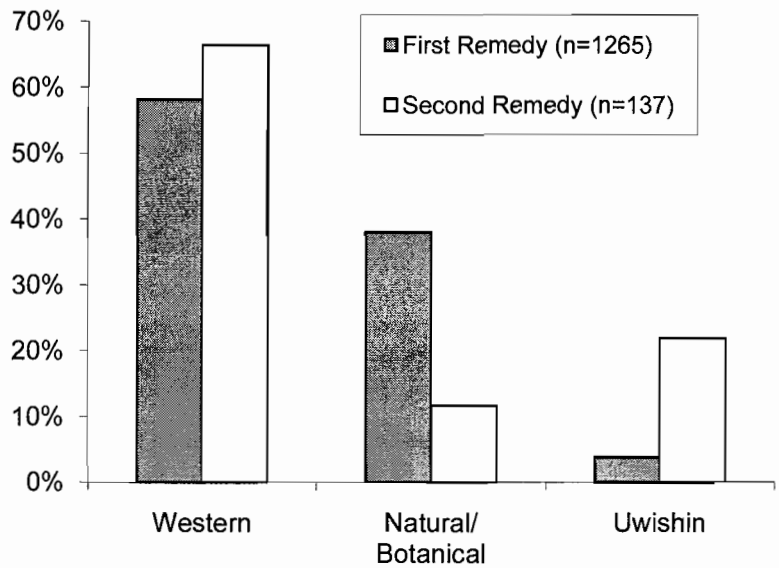

Figure 1.12. Type of treatment sought by Shuar who identified themselves as having been ill during the two weeks preceding a census survey of villages. Individuals who did not recover after seeking treatment were asked whether they sought additional treatment (second remedy). Data from the FISCH-FIPSE-FINAE Diagnostic of Shuar and Achuar Health Services and Situations. See Chapter III: Data Sources for more information.

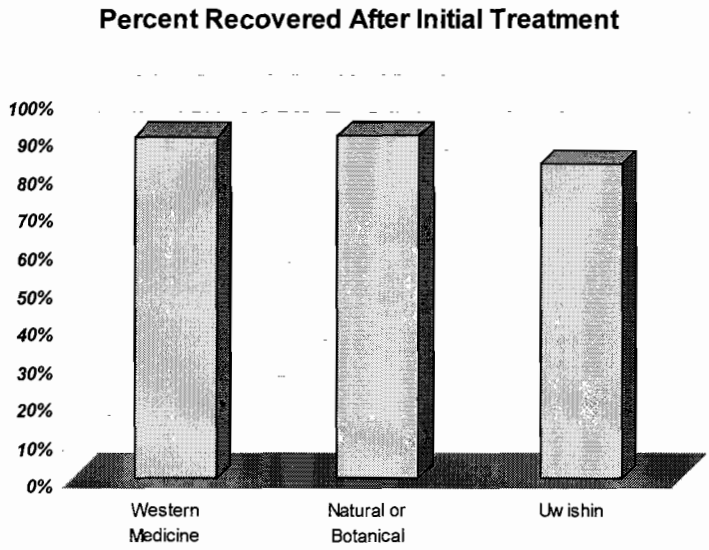

Figure 1.13. Overall recovery rates were similar regardless of the type of treatment sought. Treatments were grouped as Western (doctor, health promoter, auxiliary health promoter, aerial ambulance), natural/botanical, or shaman (uwishin). Data from the FISCH-FIPSE-FINAE Diagnostic of Shuar and Achuar Health Services and Situations. See Chapter III: Data Sources for more information.

According to the FISCH-FINAE-FIPSE survey, 86% of births occur at home. Vaccinations are becoming more common but are far from universal. About 36% of Shuar/Achuar children have been vaccinated for polio, 26% for measles, However, only 16% have received all three doses of the DPT vaccine (diphtheria, pertussis, tetanus), and only 11% have received a complete regime of vaccines (Jokisch & McSweeney, 2006).

Organization of the Dissertation

This dissertation is organized into six chapters that examine Shuar life histories, health, and immune function in the context of rapidly changing circumstances. Chapter II describes the growth of 1,384 Shuar from the Upano Valley of Ecuador and

surrounding areas, compared to 570 non-indigenous *colono* (or colonist) children from the same area, and 42 Shiwiar from the interior of Ecuador. Chapter II has been previously published in the American Journal of Human Biology, and is coauthored with George Pryor III, a graduate student who entered and organized much of the data, Jose Pozo from the Ecuadorian *Ministerio de Salud Publica*, Washington Tiwi of the Shuar Federation, who organized the diagnostic survey that collected the data, and Lawrence Sugiyama, who coordinated the data organization and entry with Tiwi, Pozo, and Pryor. We find that 40% of Shuar children can be classified as stunted, compared to less than 20% of *colonos*. Shuar are three times more likely to be stunted than *colonos* and eight times more likely to be stunted than Shiwiar. With these results, Chapter II challenges commonly held assumptions about market integration, namely, that development always means increase health and well-being for indigenous populations. Rather, the results suggest that changes have negatively affected Shuar growth and nutrition. The results also have important implications for life history theory. Shuar height is profoundly affected by circumstances, but weight is highly conserved. Chapter II concludes by discussing the trade-off between height and weight as a life history strategy.

Chapter III examines these growth outcomes in the context of QQ tradeoffs faced by parents. Few studies have unequivocally demonstrated QQ trade-offs in humans due to a number of confounds, including the fact that extending families and kin contributions may offset trade-offs in parental investment. Chapter III uses a unique pooled resource model to control for the effects of all household members simultaneously. We use data on the growth of 129 Shuar children from 56 families, sampled from 15 different villages

to test the following predictions: 1) that younger juveniles will have negative effects on one another's growth due to competition for limited resources; 2) that adult females will have positive effects on the growth of their own children; 3) that the effects of other individuals, such and fathers and adolescents, will vary based on market conditions. Chapter III finds strong evidence for a QQ trade-off, and finds that the contributions of other household members vary in complex ways as a consequence of market integration. Chapter III is coauthored with Washington Tiwi and Lawrence Sugiyama.

Chapter IV and Chapter V extend the analysis of life history trade-offs to examine the effects of market integration and household composition on the development of immune function. Chapter IV examines the age profile of Immunoglobulin E (IgE) in a Shuar village in comparison with the Tsimane of Bolivia and a representative sample from the United States. IgE is a humoral response implicated in resistance to helminths and allergic response. A number of coauthors contributed to Chapter IV. Josh Snodgrass, Felicia Madimenos, Lawrence Sugiyama, and I collected Shuar samples. Tsimane data comes from Michael Gurven and Hillard Kaplan. We find that these populations differ significantly in IgE: Tsimane have the highest (geometric mean = 6,298 IU/ml) followed by Shuar (1,196 IU/ml) and NHANES (52 IU/ml). All three populations also share similar age patterning. However, IgE peaks at different ages in each population. We find that the difference in peak IgE may reflect the phenomena known as "peak shift" whereby both infection and immunity peak earliest in populations with the highest disease transmission rate. The peak shift has long been predicted by immunoepidemiological models, but Chapter IV is the first study we are aware of to

present clear evidence of a peak shift in humoral response. The results also suggest that life history trade-offs between T_H1 and T_H2 type responses differ between these three populations.

Chapter V also presents unique research. It is the one of the first studies to test directly for life history trade-offs between multiple branches of immune function and growth. Chapter V is coauthored with Josh Snodgrass, Felicia Madimenos, Melissa Liebert, and Lawrence Sugiyama. Three studies are presented in Chapter V. The first examines the relationship between IgE, C-reactive protein (CRP, a biomarker of inflammation) and growth in Shuar children. IgE is found to be associated with poorer growth for all children. In contrast, CRP is associated with poorer growth in young children, but with better growth in older children. The results suggest a shift in the allocation of resources based on early environments. Although cross-sectional rather than longitudinal, the results are consistent with a theoretical model in which children exposed to helminths early in life shift energy from growth into specific defenses (IgE). We propose that these are the children that have high CRP at young ages, but low CRP and high IgE later in life. The second study tests whether these differences persist into adulthood, and finds that high IgE remains inversely correlated with height in Shuar adults. Finally, the third study in Chapter V examines the role of household size in determining life history allocations. We find that children from families with more dependents have higher IgE and poorer growth, while the presence of males or females over age forty has strong positive effects on both growth and the level of IgE. We suggest that older adults provide additional resources which cause increases in both

branches of the trade-off between growth and immune function, whereas children in the household increase pathogen exposure, causing siblings to shift the allocation of energy away from growth and towards immune function. Chapter V concludes by discussing these possible interpretations.

Finally, Chapter VI is a single authored chapter that synthesizes the results of the dissertation as a whole and presents general conclusions and future avenues for research.

BRIDGE TO CHAPTER II

The growth of children and juveniles is frequently used as a primary indicator of population health, so we begin our analysis of Shuar life histories and health by broadly describing the growth of Shuar children in comparison to other groups in the area, and in comparison to standards used in the United States. Although, conditions vary across Shuar territory as individual villages experience market integration differently, Chapter II sets aside within-population variation in order to examine the effects of market integration on the Shuar as a whole population. Through this broad comparison, Chapter II helps to place the Shuar within the broader context of Latin America and Ecuador, and provides a more extensive framework for the more detailed work reported in later chapters.

CHAPTER II

GROWTH AND MARKET INTEGRATION IN AMAZONIA: A COMPARISON OF GROWTH INDICATORS AMONG SHUAR, SHIWIAR, AND NON-INDIGENOUS SCHOOLCHILDREN

This chapter was previously published as: Blackwell AD, Pryor III G, Pozo J, Tiwi W, Sugiyama LS. 2009. Growth and market integration in Amazonia: A comparison of growth indicators between Shuar, Shiwiar, and nonindigenous school children. American Journal of Human Biology *21:161-171.*

The Shuar and colono *data used in this paper was collected as part of a diagnostic census by of the Federacíon Interprovincial de Centros Shuar (FICSH) and Jose Pozo of the Ministerio de Salud Pública de Morona Santiago. George Pryor, III was instrumental in organizing and entering the data. Lawrence Sugiyama organized the collaboration with Washington Tiwi and Jose Pozo and collected the Shiwiar data. The author of this dissertation was responsible for remaining work, including all data analysis, textual and graphical content, and publication.*

INTRODUCTION

Increasing integration of indigenous groups with non-native society often brings benefits such as education, economic opportunities, and access to health care. However, a growing number of studies have also documented an increase in negative chronic health outcomes such as obesity and type-2 diabetes (Baker et al., 1986; Friedlaender et al., 1987; Huss-Ashmore et al., 1992; Lindgarde et al., 2004; Lindgarde et al., 2006; Pavan et al.,

1999; Popkin, 2004; Shephard & Rode, 1996). For instance in two Amazonian populations, traditionally living individuals have healthier measures of leptin, insulin, body fat, and blood pressure compared to those with greater market integration (Lindgarde et al., 2004; Pavan et al., 1999). Many of these changes are linked to changes in diet, activity, and pathogen exposure. In some instances, increased market integration increases consumption of animal products at a cost to fruits and vegetables, as fewer crops are grown for consumption within the home and more high fat, high sugar products are purchased (Bermudez & Tucker, 2003; Rivera et al., 2004; WHO/FAO, 2003). In other instances market integration is linked to decreases in protein consumption with concomitant increases in the use of tubers or other carbohydrates, such as when hunting people move towards settled agriculture.

Dietary, economic, and demographic differences related to differing cultural practices and acculturation also affect growth outcomes in children (Bogin, 1999; Bronte-Tinkew & DeJong, 2004; Foster et al., 2005; Godoy et al., 2008; Johnston, 2002; Larrea & Kawachi, 2005; Leonard et al., 2000). In this paper we describe and compare the growth of juveniles from three groups living in Amazonian Ecuador and experiencing different degrees of market integration and acculturation. From most to least market access, these include 570 non-indigenous *colono* (or colonist) children from the Upano River Valley, 1,384 indigenous Shuar from the Upano Valley and surrounding areas, and 42 Shiwiar from the interior of Ecuador. Shuar and Shiwiar are both Jivaroan speaking groups, and traditionally lived very similar lifestyles based on hunting, fishing, and horticulture (Karsten, 1935; Stirling, 1938). However, Upano Valley Shuar today are increasingly

integrated into markets and have seen large declines in hunting due to conversion of forest to pasture, logging, and depletion of wildlife. Moreover, they live in the same environment as their non-indigenous *colono* neighbors. This situation provides an opportunity to compare people from similar cultural and ethnic backgrounds living under two different socio-ecological conditions (Shuar vs. Shiwiar), as well as people from a different cultural background living in the same ecology (Shuar vs. *colonos*). For these groups we describe height-for-age, weight-for-age, weight-for-height, BMI-for-age and growth rates relative to National Health and Nutrition Examination Survey (NHANES) references. We then compare all three groups to assess the effects of market integration and acculturation on child-juvenile growth outcomes.

METHODS

Study Populations

Shuar. Traditionally, Shuar lived in scattered households across the Upano River Valley, between the eastern Andean foothills and the Cutucu range (Figure 2.1). Early in the 20th century, introduction of firearms allowed them to expand eastward across the Cutucu into the territory of the neighboring Achuar, so that Shuar now live on both sides of the Cutucu, and throughout the Upano River Valley from the Peruvian border past the Rio Pastaza and north across the Rio Napo. Traditionally, Shuar economy was based on horticulture, hunting, and fishing (Descola, 1996; Harner, 1984; Karsten, 1935; Rubenstein, 2001; Stirling, 1938). East of the Cutucu, where there is no road access,

some Shuar continue to subsist primarily by hunting, fishing, and horticulture. However, a main road (recently paved) runs the length of the Upano valley, and Shuar are experiencing widely different effects of economic development across their territory.

In the Upano Valley, many Shuar are within walking distance of road access, live in larger communities, and have divided community lands into individually held plots (sometimes within communally held lands). Hunting and fishing are no longer critical parts of the economy, available land is limited, and land conflict between Shuar and with non-Shuar colonists (*colonos*) is a recurrent problem. Shuar of the Upano valley appear to have diets and subsistence regimes based largely on small-field horticulture, animal husbandry, and wage labor. No quantitative data based on direct observation of these aspects of Shuar economy and subsistence are currently available for the Upano Valley, although survey results (Pozo & Posligua, 2006) and our own (unpublished) interviews conducted in 2005 and 2007 support these descriptions. Results from Shuar living a few hundred kilometers to the north of the study area suggest that Shuar continue to consume significant animal protein, despite significant market integration (Lu, 2007).

Colonos. Upano Valley Shuar live adjacent to communities of *colonos*, or colonists of mixed indigenous/European descent who have moved into the area. *Colonos* in the Upano Valley area either live in town, or in small rural communities scattered across the area. *Colonos* in town, particularly around Sucúa, typically work in wage jobs, attend school, grow and purchase food and otherwise live a small-town (but not necessarily

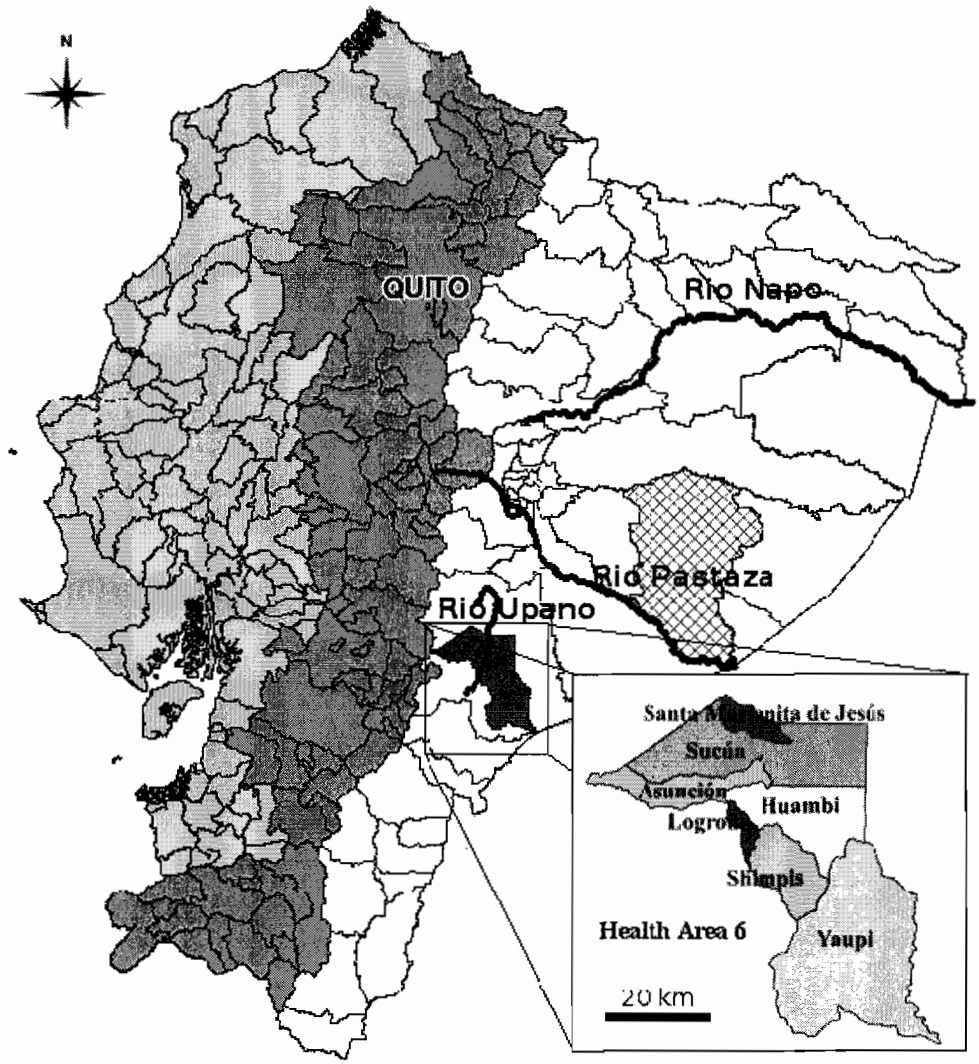

Figure 2.1. Map of Ecuador showing the three regions of the coast (light gray) the Andean highlands (medium gray) and the Amazon (white), as well as the major rivers in the area. Health Area 6 is shown in dark gray and at higher scale to show the *parroquias* it includes. The Cutucu range is not shown on the map, but runs parallel to the Upano River and divides Health Area 6 such that Yaupi lies to the east of the Cutucu, while the Upano River lies to the west. The area of Pastaza where Shiwiar data was collected is indicated with crosshatching. Maps are based on data from the *Sistema Integrado de Indicadores Sociales del Ecuador* released by the *Secretaría Técnica del Frente Social* of Ecuador.

cosmopolitan) life. Although *colonos* and Shuar live in communities that may be quite near each other (for instance a short walk across a small valley) and are not segregated by geography, ethnic tensions, sometimes fueled by conflicts over land or between the Ecuadorian authorities and the Shuar Federation, keep the Shuar community and the *colono* community largely socially and politically divided.

Shiwiar. Shiwiar are a Jivaroan speaking people closely related to the Shuar and Achuar, who live in small scattered communities in the upper Amazonian neo-tropical forests of Ecuador and northwestern Peru. At the time of study (1994-1998) Shiwiar numbered about 2000 and continued to follow traditional subsistence patterns, even more so than interior Shuar (Sugiyama, 2004; Sugiyama & Chacon, 2000). No roads entered the study area. In the rainy season, the bulk of protein came from hunting, accompanied by fishing with hook and line. Hunting was largely successful, with 73% of hunts yielding meat for an average daily per capita meat intake of 56 g (Sugiyama & Chacon, 2000). As the dry season progressed, fishing gradually increased as rivers become shallow and fishing with poison became increasingly efficient. The bulk of calories came from a wide variety of horticultural products, the most important being manioc, plantains, yams, sweet potatoes and maize. Foraging for palm heart and palm grubs was a regular contributor to the diet, which was rounded out by small amounts of seasonal wild fruits, honey, insects, frogs and other occasional foods. At the time of study the two study villages were comprised of 8 and 12 households respectively.

Data Sources

2005 School Childrens' Health Diagnostic. Shuar and *colono* data come from a previously unpublished 2005 health diagnostic conducted with the *Federacíon Interprovincial de Centros Shuar* (FICSH) and Hospital Pio XII in Sucúa, Ecuador, which included 2171 Shuar and non-Shuar school-age children living within Morona Santiago, Health Area 6 (Figure 2.1). Our collaboration with this study and use of this data was approved by the University of Oregon Institutional Review Board and by FICSH. A physical and dental exam was administered at village schools by four medical teams comprised of a physician, dentist, and two nurses or nurse auxiliaries. Height was measured using a standard metric tape measure attached to a vertical surface. Weight was measured using a standard bathroom scale.

The sample includes nearly 100% of children attending school on the day of the team's visit, as well as a few non-attendees. Although we cannot state the exact percentage of the population represented, most children attend school so it is expected to be near 100% for elementary school age children. Ages were available for 2110 individuals (range = 1-17 years, mean = 8.3 ± 2.6). The majority of children were elementary-school age; only 4% were younger than five, and only 2% older than thirteen (Table 1). Children's ethnicity was assessed based on self-report and community membership. Some communities are exclusively Shuar since FISCH law bans the sale of Shuar lands to non-Shuar. The sample includes 1384 Shuar children (52% male, 48% female). Of these, 92.5% were from the Upano Valley, with the majority (65% of the total) living in Sucúa *parroquia* (Figure 2.1). The remaining 7.5% were from Yaupi

parroquia, which lies across the Cutucu from the Upano Valley (Figure 2.1). The sample also includes 570 *colonos* from the Upano Valley (56% male, 44% female). Excluded from analyses were 245 children of unknown (52 children) or other ethnicities (193 children, most of whom were listed as *mestizo*, or mixed ethnicity).

1994-1998 Shiwiar Data. Shiwiar health and anthropometric data were gathered by Sugiyama during separate field trips in two communities between 1994 and 1998. Shiwiar data was collected from the villages of Alto Corrientes and Kurintza, located in the region of Pastaza indicated in Figure 2.1. The dataset includes 42 Shiwiar children under age 18, including 25 males between the ages of 3 and 12 and 16 females between the ages of 2 and 18. Anthropometric measures were collected as part of a larger health study, and additional details have been described elsewhere (Sugiyama, 2004; Sugiyama & Scalise Sugiyama, 2003). Briefly, height was measured using a standard portable stadiometer. Weight was measured by having subjects sit in a hammock suspended from a 100 or 50 kg spring scale. Height was available for 36 individuals and weight for 21. Ages are based on informant reports and/or birth records, such that at least year of birth was known for all individuals.

Analysis

Growth reference z-scores were calculated from National Health and Nutrition Examination Survey (NHANES) LMS data files available from the National Center for Health Statistics at the Center for Disease Control (www.cdc.gov/growthcharts/) and based on references developed in the year 2000. The LMS data files contain values for

the median (M), generalized coefficient of variation (S), and Box-Cox power (L) by age or stature, as appropriate for the measure. These were used to convert Shuar, *colono*, and Shiwiar BMI, weight, and height to z-scores according to the equation $Z = ((X/M)^L - 1)/(LS)$, where X is the measure in question (Box & Cox, 1964; Cole TJ, 1990). NHANES references include ages 2-20 for weight, height, and BMI, as well as weight-for-heights standards for individuals between 77 and 121 cm. Thus, some individuals in our data were excluded from analysis because they were outside of reference ranges, and sample size and composition differ slightly depending on the measure under analysis.

Using these standards, we defined *stunting* as a height-for-age z-score $\leq$ -2, *wasting* as a weight-for-height z-score $\leq$ -2, *underweight* as a weight-for-age z-score $\leq$ -2, and *low BMI* as a BMI-for-age z-score $\leq$ -2. Two-tailed, one sample t-tests were used to compare mean z-scores with zero. Independent samples t-tests assuming equal variances were used to compare scores by sex. ANCOVA and binary logistic regression were used to compare groups while controlling for age and sex. All calculations and analysis were done using SPSS 15.0 (SPSS Inc.).

Z-scores were also calculated based on World Health Organization (WHO) references available from the WHO (http://www.who.int/childgrowth/en/). The use of WHO z-scores yielded qualitatively similar results to the use of NHANES standards, reported below, so results with WHO references are not reported in this paper. However, they are included in Appendix A.

RESULTS

Comparison between Shuar and Colono Children

Shuar children's growth. Shuar children's mean height, weight, and BMI by age and sex are listed in Tables 2.1 and 2.2, and illustrated graphically in Figures 2.2 and 2.3. Compared to NHANES growth references, mean z-scores for Shuar children were significantly below zero for height-for-age (HAZ) and weight-for-age (WAZ) (Table 2.5). Stunting was prevalent in both males (41%) and females (38%). Underweight was less common (males: 14%, females: 15%). Conversely, mean z-scores for BMI-for-age (BAZ) and weight-for-height (WHZ) were significantly higher than zero for both sexes (males: 0.18 and 0.41, respectively; females: 0.14 and 0.24, $p < 0.01$ for all tests). Low BMI was uncommon (males 6%, females 3%) as was wasting (males 8%, females 5%).

Comparing males and females, there were no significant differences in mean z-scores (all t-tests, $p > 0.05$). When we examine results by age cohorts, prevalence of stunting appears to increase with age, particularly in males (Table 2.1). Prevalence of wasting appears to decrease with age, and to be common only in children age under four (Tables 2.1 and 2.2). To separate the effects of age and sex on Shuar z-scores, we used multiple ANCOVAs with age, sex, and an age by sex interaction term as independent variables. HAZ was found to decrease with age for both sexes ($\beta = -0.08$, $t = -4.44$, $p < 0.01$) as did WAZ ($\beta = -0.04$, $t = -2.22$, $p = 0.03$). WHZ increased with age for both sexes ($\beta = 0.14$, $t = 3.43$, $p < 0.01$). There was no significant effect of age on BAZ. The only significant main effect of sex was on WAZ, with males having higher z-scores than females ($\beta = 0.51$, $t = 2.36$, $p = 0.02$). For WAZ there was also a significant interaction

between sex and age, with males decreasing more with age ($\beta = -0.06$, $t = -2.56$, $p = 0.01$). A similar, but not quite significant interaction was observed for HAZ ($\beta = -0.05$, $t = -1.88$, $p = 0.06$).

Colono children's growth. Mean *colono* growth measures by age cohort are shown in Tables 2.3 and 2.4, and presented graphically in Figures 2.2 and 2.3. Like the Shuar, *colono* children had mean HAZ and WAZ significantly below zero (Table 2.5). Only male *colonos* had mean WHZ significantly above zero (Table 2.5). Sixteen percent of *colono* males and 20% of *colono* females could be classified as stunted. Underweight was not very prevalent among *colono* children (9% for males and 12% for females). Low BMI was uncommon (8% for males, 7% for females) as was wasting (7% for males, 6% for females) (Table 2.5). No measured differences between male and female *colonos* were significant (all t-tests, $p > 0.05$).

By age cohort, stunting becomes more prevalent in *colono* children with age (Tables 2.3 and 2.4). Using multiple ANCOVAs as with the Shuar, HAZ decreased with age ($\beta = -0.16$, $t = -5.57$, $p < 0.01$) as did WAZ ($\beta = -0.12$, $t = -3.57$, $p < 0.01$). BAZ and WHZ were not significantly affected by age. However, there are few young *colono* children in the sample, which may obscure early wasting. There was no significant main effect of sex on any z-score, nor any significant interaction between sex and age.

Table 2.1. Male Shuar mean growth outcomes, z-scores, and sample sizes by sex and yearly age cohort

		Height-for-age			Weight-for-age			BMI-for-age			Weight-for-height		
Age	**n**	**Mean (cm)**	**Mean z**	**% z ≤ -2**	**Mean (kg)**	**Mean z**	**% z ≤ -2**	**Mean BMI**	**Mean z**	**% z ≤ -2**	**n**	**Mean z**	**% z ≤ -2**
0	4	67.0	-	-	7.3	-	-	18.2	-	-	-	-	-
1	5	72.6	-	-	8.1	-	-	15.4	-	-	-	-	-
2	4	84.9	-0.57	0%	10.5	-1.84	50%	14.6	-1.89	75%	4	-2.06	75%
3	6	97.3	0.29	0%	14.3	-0.35	17%	15.1	-1.05	33%	6	-0.98	17%
4	13	96.1	-1.78	54%	16.0	-0.63	23%	17.2	0.99	8%	13	0.61	15%
5	58	103.8	-1.29	31%	17.8	-0.55	7%	16.5	0.58	7%	57	0.41	9%
6	97	109.2	-1.31	26%	19.6	-0.65	12%	16.3	0.37	7%	94	0.27	7%
7	97	113.1	-1.67	37%	21.1	-0.88	12%	16.4	0.29	6%	88	0.35	8%
8	98	117.7	-1.87	42%	23.3	-0.85	9%	16.8	0.36	5%	78	0.52	6%
9	79	123.2	-1.78	41%	26.0	-0.80	10%	17.1	0.30	3%	32	0.99	0%
10	79	127.1	-1.82	42%	27.7	-1.06	16%	17.1	-0.02	3%	13	0.84	0%
11	56	130.4	-1.96	57%	29.9	-1.26	13%	17.5	-0.06	5%	7	1.05	0%
12	39	133.6	-2.20	64%	30.4	-1.87	33%	17.1	-0.84	15%	3	0.90	0%
13	26	137.8	-2.42	65%	35.3	-1.66	42%	18.5	-0.16	4%	1	-0.44	0%
14	12	142.5	-2.50	58%	43.6	-0.93	9%	20.2	0.32	0%	-	-	-
15	7	154.3	-1.91	43%	52.5	-0.57	0%	21.9	0.48	0%	-	-	-
16	2	149.5	-2.97	100%	44.0	-2.23	50%	19.6	-0.37	0%	-	-	-
17	1	138.6	-4.67	100%	41.8	-3.29	100%	21.8	0.18	0%	-	-	-

Table 2.2. Female Shuar mean growth outcomes, z-scores, and sample sizes by sex and yearly age cohort

		Height-for-age			Weight-for-age			BMI-for-age			Weight-for-height		
Age	**n**	**Mean (cm)**	**Mean z**	**% z ≤ -2**	**Mean (kg)**	**Mean z**	**% z ≤ -2**	**Mean BMI**	**Mean z**	**% z ≤ -2**	**n**	**Mean z**	**% z ≤ -2**
Females													
0	1	.	-	-	5.0	-	-	.	-	-	-	-	-
1	6	72.6	-	-	8.9	-	-	17.2	-	-	-	-	-
2	3	85.4	-0.52	0%	11.3	-1.00	0%	15.5	-0.62	0%	3	-0.82	33%
3	5	85.9	-2.37	60%	11.4	-2.19	40%	15.6	-0.49	20%	4	-1.17	50%
4	9	96.4	-1.41	44%	15.5	-0.63	22%	16.5	0.77	0%	9	0.37	0%
5	71	103.1	-1.11	23%	17.2	-0.62	14%	16.1	0.28	7%	71	0.06	7%
6	83	108.2	-1.41	33%	18.9	-0.72	8%	16.1	0.32	6%	83	0.20	6%
7	85	112.6	-1.78	35%	20.5	-0.93	15%	16.1	0.19	2%	82	0.22	5%
8	84	117.1	-1.94	45%	22.4	-1.00	11%	16.4	0.08	4%	73	0.33	4%
9	73	121.4	-1.99	52%	25.1	-1.05	22%	16.9	0.14	0%	39	0.44	0%
10	74	127.8	-1.62	38%	28.3	-1.00	12%	17.3	0.03	1%	14	0.66	0%
11	55	134.5	-1.36	20%	32.1	-1.02	18%	17.6	-0.11	4%	3	1.34	0%
12	38	138.5	-1.73	37%	36.3	-0.89	8%	18.9	0.08	3%	-	-	-
13	20	139.3	-2.59	65%	37.8	-1.25	25%	19.6	0.09	0%	1	3.20	0%
14	8	142.4	-2.75	88%	42.8	-0.99	11%	21.3	0.32	0%	-	-	-
15	3	149.3	-1.95	33%	46.2	-0.92	25%	20.0	-0.04	0%	-	-	-
16	1	136.0	-4.13	100%	39.0	-2.55	100%	21.1	0.20	0%	-	-	-
17	-		-	-		-	-		-	-	-	-	-

Table 2.3. Male *colono* mean growth outcomes, z-scores, and sample sizes by sex and yearly age cohort

		Height-for-age			Weight-for-age			BMI-for-age			Weight-for-height		
Age	**n**	**Mean (cm)**	**Mean z**	**% z ≤ -2**	**Mean (kg)**	**Mean z**	**% z ≤ -2**	**Mean BMI**	**Mean z**	**% z ≤ -2**	**n**	**Mean z**	**% z ≤ -2**
0	-	-	-	-	-	-	-	-	-	-	-	-	-
1	-	-	-	-	-	-	-	-	-	-	-	-	-
2	1	85.0	-1.36	0%	13.7	0.28	0%	19.0	1.70	0%	1	1.46	0%
3	-	-	-	-	-	-	-	-	-	-	-	-	-
4	14	101.6	-0.71	7%	16.8	-0.22	7%	16.2	0.39	0%	14	0.22	0%
5	45	106.3	-0.67	11%	18.4	-0.23	5%	16.2	0.44	5%	44	0.30	5%
6	30	112.7	-0.59	10%	21.4	-0.08	11%	16.7	0.33	12%	24	0.20	13%
7	22	117.9	-0.77	9%	23.3	-0.15	5%	16.7	0.49	0%	16	0.46	0%
8	81	123.3	-0.85	11%	24.6	-0.60	9%	16.1	-0.26	10%	33	-0.10	15%
9	46	127.8	-0.98	22%	28.2	-0.44	13%	17.1	-0.07	13%	9	0.71	0%
10	31	131.2	-1.19	26%	31.3	-0.40	7%	18.1	0.28	3%	1	1.06	0%
11	28	134.4	-1.36	21%	34.1	-0.56	9%	18.7	0.22	4%	-	-	-
12	14	137.7	-1.63	43%	33.8	-1.20	25%	17.8	-0.33	17%	1	1.51	0%
13	3	142.3	-1.80	33%	36.0	-1.43	33%	17.7	-0.49	0%	-	-	-
14	-	-	-	-	-	-		-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 2.4. Female *colono* mean growth outcomes, z-scores, and sample sizes by sex and yearly age cohort

		Height-for-age			Weight-for-age			BMI-for-age			Weight-for-height		
Age	**n**	**Mean (cm)**	**Mean z**	**% z ≤ -2**	**Mean (kg)**	**Mean z**	**% z ≤ -2**	**Mean BMI**	**Mean z**	**% z ≤ -2**	**n**	**Mean z**	**% z ≤ -2**
0	1	65.0	-	-	7.5	-	-	17.8	-	-	-	-	-
1	1	77.0	-	-	8.8	-	-	14.8	-	-	1	-1.94	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-
3	1	91.0	-0.82	0%	13.5	-0.27	0%	16.3	0.46	0%	1	0.16	0%
4	8	101.6	-0.45	13%	17.3	0.23	0%	16.8	0.95	0%	8	0.75	0%
5	39	107.0	-0.36	5%	18.2	-0.16	5%	15.9	0.31	8%	37	0.12	8%
6	30	111.5	-0.72	17%	19.8	-0.30	5%	15.5	-0.09	5%	21	-0.24	5%
7	23	116.3	-1.05	22%	23.1	-0.20	9%	16.9	0.50	5%	19	0.35	5%
8	23	120.0	-1.40	26%	23.0	-0.85	13%	15.9	-0.07	0%	16	-0.04	0%
9	49	127.6	-0.92	20%	26.9	-0.75	19%	16.4	-0.44	13%	10	-0.48	20%
10	31	131.1	-1.12	10%	30.2	-0.76	17%	17.3	-0.21	10%	1	2.64	0%
11	16	135.3	-1.24	13%	34.7	-0.56	13%	18.8	0.29	0%	1	1.55	0%
12	13	140.8	-1.43	46%	37.5	-0.73	0%	18.8	0.06	8%	-	-	-
13	7	137.9	-2.77	86%	37.1	-1.47	43%	19.4	-0.12	0%	-	-	-
14	1	143.0	-2.66	100%	47.0	-0.28	0%	23.0	0.96	0%	-	-	-
15	-	-	-	-	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-	-	-	-	-

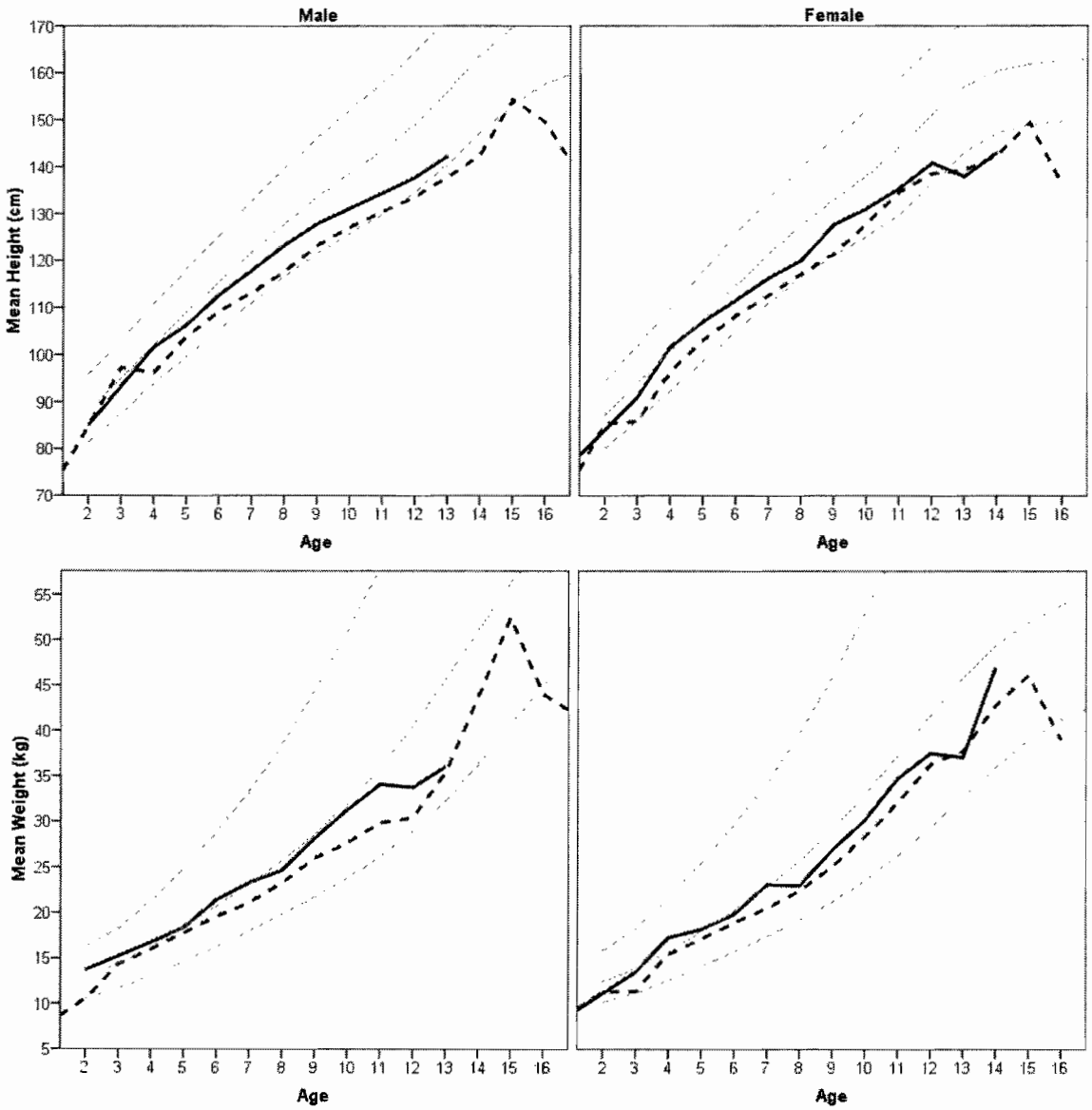

Figure 2.2. Mean weight and height by age and sex cohort for *colono* (solid black line) and Shuar (long dashes) children. For comparison, NHANES standard z-scores of 0, +2, and -2 are shown in gray. In the dataset most ages were reported in whole years. Those that were not were rounded down to the nearest year before graphing. See Tables 2.1-2.4 for sample sizes and cohort values.

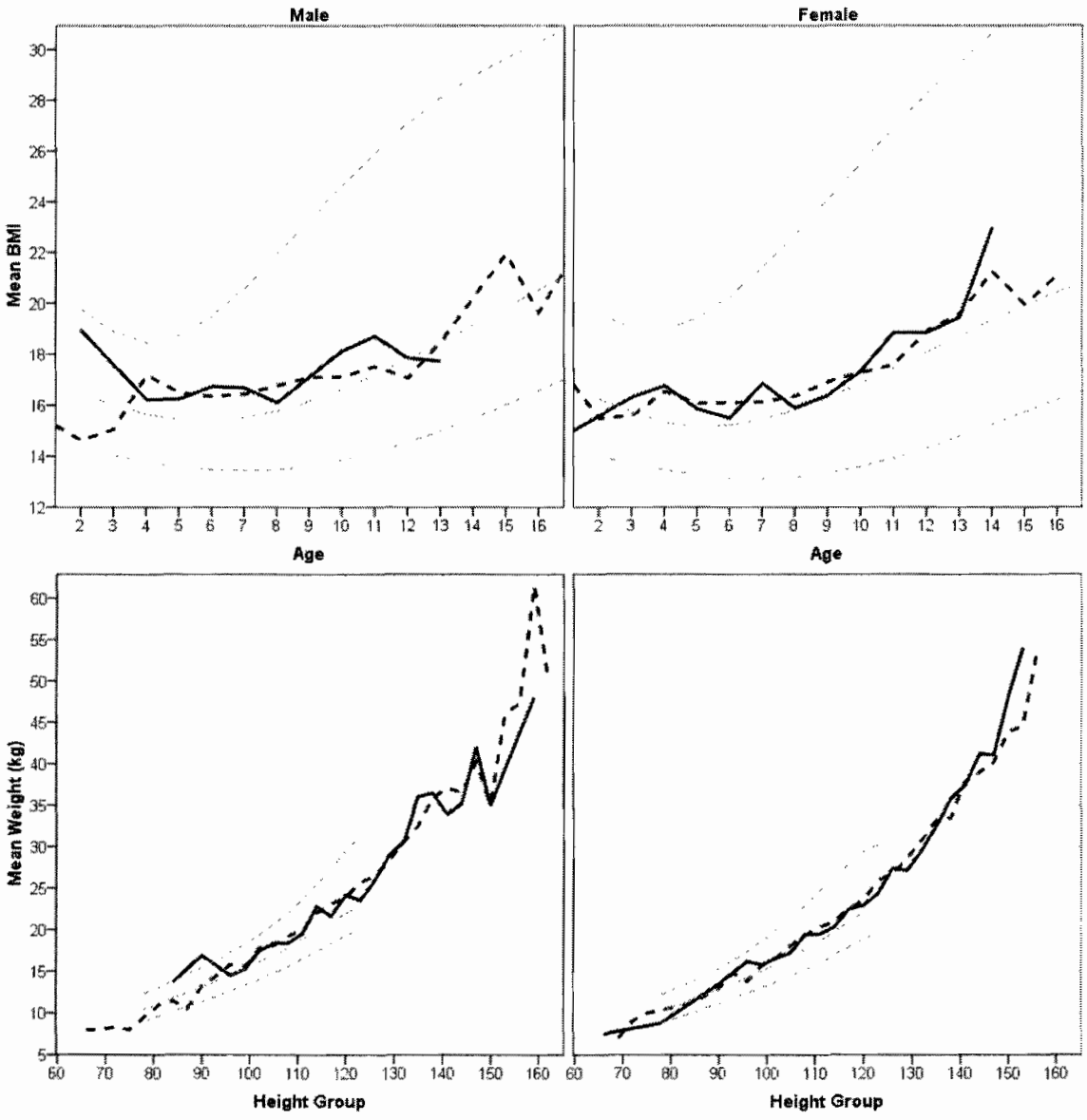

Figure 2.3. Mean BMI by yearly age cohort and weight by height for male and female *colono* (solid black line) and Shuar (long dashes) children. NHANES standard z-scores of 0, +2, and -2 are shown in gray. To smooth lines, ages were rounded down to the nearest year and heights to increments of 3 cm. See Tables 2.1-2.4 for sample sizes and cohort values.

Table 2.5. Summary of growth outcome z-scores

		N	Percent $z \leq -2$	Percent $z \geq 2$	Mean z-score	S.D.	t*	p**
Shuar								
Males	Height-for-age	674	41%	0%	-1.73	1.15	-39.12	<0.01
	Weight-for-age	672	14%	0%	-0.95	1.16	-21.26	<0.01
	BMI-for-age	671	6%	2%	0.18	1.40	3.29	<0.01
	Weight-for-height	398	8%	3%	0.41	1.39	5.90	<0.01
Females	Height-for-age	612	38%	0%	-1.68	1.21	-34.30	<0.01
	Weight-for-age	614	15%	0%	-0.92	1.13	-20.31	<0.01
	BMI-for-age	612	3%	2%	0.14	1.08	3.24	<0.01
	Weight-for-height	385	5%	4%	0.24	1.23	3.88	<0.01
Colono								
Males	Height-for-age	315	16%	1%	-0.93	1.09	-15.17	<0.01
	Weight-for-age	303	9%	1%	-0.43	1.21	-6.23	0.01
	BMI-for-age	302	8%	5%	0.10	1.39	1.25	0.21
	Weight-for-height	143	7%	6%	0.25	1.31	2.25	0.03
Females	Height-for-age	241	20%	0%	-0.98	1.14	-13.42	<0.01
	Weight-for-age	230	12%	0%	-0.54	1.16	-7.00	<0.01
	BMI-for-age	229	7%	1%	0.02	1.33	0.26	0.80
	Weight-for-height	116	6%	2%	0.06	1.19	0.55	0.58

*A one-sample t-test was used to determine whether mean z-scores differed significantly from zero. **P-values are 2-tailed

Comparison between Shuar and colono children. Figure 2.2 suggests that Shuar children have lower weights-for-age and heights-for-age than *colono* children, regardless of sex or age. Figure 2.3 suggests no systematic differences for BMI-for-age and weight-for-height. Statistical comparisons support these qualitative observations. We performed a series of ANCOVAs with age as a covariate, sex and ethnicity as factors, and all two and three way interactions included. Ethnicity had a significant main effect on HAZ ($F = 23.19$, 1 df, $p < 0.01$) and WAZ ($F = 10.38$, 1 df, $p < 0.01$), with *colono* children having higher z-scores on both. Age had a significant main effect on HAZ ($F = 101.72$, 1 df, $p < 0.01$), WAZ ($F = 48.02$, 1 df, $p < 0.01$), and BAZ ($F = 18.27$, 1 df, $p < 0.01$), all of which

decreased with age for both Shuar and *colono* children. Age also had a significant main effect on WHZ, which increased with age ($F = 6.84$, 1 df, $p = 0.01$). For HAZ there was a nearly significant 3-way interaction between ethnicity, sex, and age ($F = 3.28$, 1 df, $p = 0.07$) corresponding to a smaller age-related decrease in HAZ for Shuar females than for Shuar males or *colonos* of either sex. There was also a significant interaction between ethnicity and age on WHZ ($F = 6.24$, 1 df, $p = 0.01$) since Shuar increased in WHZ with age, whereas *colono* children did not.

To make these results more easily interpretable and to estimate the actual z-score differences associated with ethnicity, we performed separate ANCOVAs for males and females (Table 4). For males, the estimated HAZ difference between *colonos* and Shuar was 0.67, expressed in the model as the beta coefficient controlling for age and sex. For females the HAZ difference between *colonos* and Shuar was 1.32. Male Shuar and *colonos* did not differ in WAZ, but for females being a *colono* increased WAZ by 1.00. For both sexes age was related to decreases in HAZ and WAZ, and for males, BAZ (Table 2.5). However, being *colono* interacted with age, such that *colono* females had greater age related decreases in HAZ and WAZ than did Shuar females. Age was also related to increases in WHZ, but only for Shuar. Being *colono* interacted with age to cancel the overall age related increase in the model (Table 2.6).

Comparison with a Sample of Shiwiar Children

Data on a small sample of Shiwiar children was available for comparison with

Table 2.6. ANCOVAs with NHANES z-scores as dependent variables

		Males						Females					
Dependent	**Parameter**	**β**	**β 95% CI**		**SE**	**t**	**p**	**β**	**β 95% CI**		**SE**	**t**	**p**
Height-for-age	**Intercept**	-0.64	(-0.92	-0.36)	0.14	-4.48	<0.01	-0.99	(-1.31	-0.68)	0.16	-6.12	<0.01
	Colono vs. Shuar	0.67	(0.13	1.21)	0.27	2.45	0.01	1.32	(0.71	1.94)	0.31	4.23	<0.01
	Age	-0.13	(-0.16	-0.10)	0.02	-7.99	<0.01	-0.08	(-0.12	-0.05)	0.02	-4.39	<0.01
	Colono x Age	0.01	(-0.05	0.07)	0.03	0.28	0.78	-0.08	(-0.15	-0.01)	0.04	-2.16	0.03
Weight-for-age	**Intercept**	-0.08	(-0.38	0.22)	0.15	-0.54	0.59	-0.59	(-0.90	-0.28)	0.16	-3.78	<0.01
	Colono vs. Shuar	0.38	(-0.20	0.96)	0.30	1.29	0.20	1.00	(0.39	1.60)	0.31	3.24	<0.01
	Age	-0.10	(-0.14	-0.07)	0.02	-5.98	<0.01	-0.04	(-0.08	0.00)	0.02	-2.22	0.03
	Colono x Age	0.01	(-0.06	0.08)	0.04	0.30	0.76	-0.08	(-0.15	0.00)	0.04	-2.10	0.04
BMI-for-age	**Intercept**	0.77	(0.41	1.13)	0.18	4.20	0.00	0.40	(0.08	0.71)	0.16	2.46	0.01
	Colono vs. Shuar	-0.07	(-0.77	0.64)	0.36	-0.18	0.85	0.18	(-0.44	0.80)	0.32	0.56	0.58
	Age	-0.07	(-0.11	-0.03)	0.02	-3.38	<0.01	-0.03	(-0.07	0.01)	0.02	-1.66	0.10
	Colono x Age	-0.01	(-0.09	0.08)	0.04	-0.14	0.89	-0.04	(-0.11	0.04)	0.04	-0.99	0.32
Weight-for-height	**Intercept**	-0.66	(-1.22	-0.11)	0.28	-2.34	0.02	-0.71	(-1.24	-0.18)	0.27	-2.65	0.01
	Colono vs. Shuar	0.92	(-0.16	1.99)	0.55	1.68	0.09	0.74	(-0.32	1.80)	0.54	1.37	0.17
	Age	0.16	(0.08	0.24)	0.04	3.92	<0.01	0.14	(0.06	0.22)	0.04	3.65	<0.01
	Colono x Age	-0.16	(-0.32	0.00)	0.08	-1.93	0.05	-0.13	(-0.29	0.03)	0.08	-1.62	0.11

Shuar and *colono* children. The sample included 42 Shiwiar children under age 18, including 25 males and 16 females. Since the sample is small we did not have enough power to provide useful Shiwiar data by age as sex cohort, as was done with the Shuar and Shiwiar data. However, the sample is sufficient to make age and sex controlled comparisons between ethnic groups.

We used ANCOVA to estimate the mean z-score differences between Shiwiar and the other two groups of children while controlling for age and sex differences in the two samples. Shuar had significantly lower z-scores than Shiwiar in HAZ ($\beta = -0.84$, $t = -3.40$, $p < 0.01$) and WAZ ($\beta = -0.75$, $t = -3.88$, $p < 0.01$), but *colono* and Shiwiar did not differ significantly from one another in either measure. In contrast, Shuar and Shiwiar did not differ significantly in BAZ, while there was a trend for *colono* children to be lower in BAZ than Shiwiar ($\beta = -0.54$, $t = -1.83$, $p = 0.07$). *Colono* children were also significantly lower than Shiwiar in WHZ ($\beta = -0.89$, $t = -2.03$, $p = 0.04$). There was also a trend for Shuar children to have lower WHZ than Shiwiar ($\beta = -0.78$, $t = -1.80$, $p = 0.07$).

Finally, we used logistic regression to calculate odds-ratios (OR) for effects of age, ethnicity, and sex on likelihood of z-scores ≤ -2 for the four growth measures, comparing all three ethnic groups (Table 2.7). Ethnicity had a significant impact on the likelihood of stunting, with *colono* children being about three times less likely to be stunted than Shuar children (OR = 0.33; CI: 0.26 – 0.43, $p < 0.01$) and Shiwiar children being about eight times less likely to be stunted than Shuar (OR = 0.13, CI: 0.03 – 0.56, $p = 0.01$).

Table 2.7. Binary logistic regressions

Dependent	Factor	OR	95% C.I. for OR		p
			Lower	Upper	
Stunting	Colono vs. Shuar	0.33	0.26	0.43	<0.01
(Low height-for-age)	Shiwiar vs. Shuar	0.13	0.03	0.56	0.01
	Male vs. Female	1.06	0.86	1.29	0.59
	Age (per year)	1.17	1.13	1.22	<0.01
	Constant	0.17			<0.01
Low weight-for-age	Colono vs. Shuar	0.71	0.52	0.98	0.04
	Shiwiar vs. Shuar	0.31	0.07	1.31	0.11
	Male vs. Female	0.93	0.71	1.23	0.62
	Age (per year)	1.11	1.06	1.18	<0.01
	Constant	0.07			<0.01
Low BMI-for-age	Colono vs. Shuar	1.45	0.95	2.20	0.09
	Shiwiar vs. Shuar	1.06	0.14	8.09	0.96
	Male vs. Female	1.65	1.08	2.51	0.02
	Age (per year)	0.91	0.83	0.99	0.03
	Constant	0.08			<0.01
	Colono vs. Shuar	0.87	0.49	1.55	0.64
Wasting	Shiwiar vs. Shuar	0.00	0.00	.	1.00
(Low weight-for-height)	Male vs. Female	1.41	0.85	2.35	0.18
	Age (per year)	0.74	0.63	0.86	<0.01
	Constant	0.42			0.12

DISCUSSION

Our results describe the growth of three distinct but related ethnic groups living in the Ecuadorian Amazon: Upano Valley Shuar living in relatively acculturated circumstances, *colonos* living in the same geographical area as many of the Shuar considered, and Shiwiar living traditionally. Although the Shiwiar sample is limited, the Shuar and *colono* samples are both large and likely accurate. Measurements were taken by medical teams composed of doctors and nurses, and data collection was observed first hand by Sugiyama for a sample of communities. The ages of children are also likely to be accurate, since these children attend school and records exist for their birth dates.

While it is worth noting that ages given in school records were not re-checked against birth records to verify accuracy, the children themselves and/or their siblings served as a cross-check on the accuracy of the recorded ages.

Despite the large sample, the Shuar and *colono* samples do have some limitations which should be noted. First, the use of standard bathroom scales and tape measures may have introduced some errors relative to more accurate instruments. Second, the ages represented in the sample are limited. There are very few children younger than four or older than thirteen in the sample. Thus, the sample is not very informative with regard to the timing of adolescent growth, nor with regard to growth in the first few years of life. These limitations should be taken into account when drawing conclusions from these data.

The strongest finding from this study is that Shuar children have higher prevalence of stunting than either of the other two groups considered. About 40% of the Shuar children in this study were classified as stunted. In contrast, only about 18% of the *colono* children had z-scores indicative of stunting. The odds of stunting for Shuar were three times greater than the odds for stunting for *colonos* and eight times the odds for the Shiwiar. In terms of z-scores, Shuar were exceeded by both *colono* and Shiwiar. Shuar also had relatively high levels of underweight for age, around 15%. This is higher than the 6.2% reported for Ecuador as a whole (World Health Organization, 2007), but lower than the median prevalence of 22.8% reported for the entirety of Latin America (Victora, 1992).

Human growth is highly plastic and growth in height is strongly influenced by environmental and social factors which impact nutrition and disease (Benefice *et al.*, 2006; Bogin, 1999; Bogin & Loucky, 1997; Bronte-Tinkew & DeJong, 2004; Foster *et al.*, 2005; Godoy *et al.*, 2008; Johnston, 2002; Leonard *et al.*, 2000; Norgan, 2002; Schell & Knutsen, 2002; Victora, 1992; Walker *et al.*, 1996). For example, rainfall during early childhood has been linked to adult height outcomes in Bolivia (Godoy *et al.*, 2008) and a number of factors, including maternal schooling, indigenous status, tuber consumption, maternal fertility, and economic inequality correlate with height across a broad sample in Ecuador (Larrea & Kawachi, 2005). Among Shuar, tradeoffs have been found between family size and the height and weight of offspring (Hagen *et al.*, 2006). Therefore differences between *colono*, Shuar, and Shiwiar are likely attributable to cultural and environmental differences, rather than genetic factors. This is particularly likely to be the case for the comparison between Shiwiar and Shuar children who are ethnically and culturally linked, but who experience different degrees of acculturation based on their geographical proximity to market economies and availability traditional resources such as forest game. Further evidences comes from comparison with the Achuar, who are closely related to the Shuar, and of which the Shiwiar we report on can be considered a less acculturated subgroup. Among male Achuar under age seventeen, 29% of males and 19% of females were stunted (Orr *et al.*, 2001), compared to 41% of male and 38% of female Shuar in this study.

The high prevalence of stunting among Upano Valley Shuar is comparable to the prevalence reported for many other South American groups. Among the Tsimane of

Bolivia, prevalences of stunting between 40-50% have been reported (Benefice *et al.*, 2006; Foster *et al.*, 2005). In Ecuador as a whole, 25-30% of children under age five are reported to be stunted, with a prevalence of 58% for all indigenous groups combined (Larrea & Kawachi, 2005; World Health Organization, 2007). In contrast, Shuar prevalence of stunting is considerably lower than that for other indigenous South American groups, such as the Tukanoan of Columbia (Orr *et al.*, 2001) and Chachi of Ecuador (Stinson, 1989), both of which have stunting prevalence ranging from 70%-82%.

It has been suggested that the Achuar have relatively low levels of stunting because they have one of the highest protein intakes recorded among native Amazonians (Descola, 1994; Orr *et al.*, 2001; Sugiyama & Chacon, 2000). The fact that Upano Valley Shuar have higher levels of stunting suggests that acculturation is negatively impacting protein levels, perhaps by replacing hunted food with more tubers, rice, and other carbohydrate rich foods, or with purchased sources of protein that are infrequently available. Although at present we do not have quantitative data to test this hypothesis, preliminary food frequency and open-ended interview data supports this view: in the Upano Valley hunting is relatively infrequent, game is scarce, and purchased meats infrequent in the diet. Acculturation may also decrease traditional activities such as the sharing of meat between families, such as has occurred among the Tsimane (Brabec *et al.*, 2007).

Considering the overall prevalences of wasting in all three ethnic groups we found few surprises. Wasting and low BMI-for-age were uncommon in all three groups, affecting < 8% of children. This pattern of high stunting prevalence with low prevalence

of wasting is common across Latin America (Godoy *et al.*, 2005). Victora (1992) compiled 37 studies from Latin America and found that the median prevalence of stunting was 34% whereas the median prevalence of wasting was only 3%. However, Shuar prevalences of wasting are strongly linked to age and are much higher in younger age cohorts, particularly those under five. This could be the product of sampling bias, since our sample of Shuar under age five is small and we lack a complete comparative sample of young *colono* or Shiwiar. However, two things lead us to suspect this finding may be real. First, there is a steady decrease in wasting prevalence with age, suggesting a consistent pattern. Second, both male and female Shuar show similar patterns of stunting. Nevertheless, these patterns could be the result of consistent bias, for example if sick children were more likely to be included due to parents bringing them to see the doctors and nurses during data collection. Thus, any conclusions about wasting in young Shuar children should be considered tentative.

It is frequently suggested that stunting represents chronic undernutrition or pathogen costs, whereas wasting is an indicator of short term lack—since weight can fluctuate over relatively short periods of time (Fernandez *et al.*, 2002; Walker *et al.*, 1996). Thus, wasting and underweight are seen as preceding stunting. However, some, such as Victora (1992) argue against this simple picture, suggesting that stunting and wasting may have distinct etiologies based on limiting factors besides energy availability, such as the availability of specific nutrients.

Our results support this view, at least in terms of the short-term connection between stunting and wasting. For the Shuar in our sample, HAZ is negatively correlated

with WHZ ($r = -0.14$, $p < 0.01$), suggesting that the same individuals are not both stunted and wasted. This is largely due to fact that HAZ decreases with age, while WHZ increases. Controlling for age and sex, HAZ and WHZ are not significantly correlated ($r = -0.04$, $p = 0.28$). If stunting were the consequence of persistent or repeated periods of wasting, we would expect a positive correlation, albeit possibly a weak one. Since the age-related patterns of wasting and stunting are opposite to one another, either separate factors must limit height growth and weight growth or the connection between stunting and wasting must be long-term rather than short-term.

For example, stunting might result from insults during sensitive periods, such as during infancy or weaning. Considered by itself, stunting does not appear to be the effect of insults early in life, since height-for-age z-scores decrease with age. However, considered with weight-for-height z-scores this seems plausible. Early wasting might lead to later stunting by shifting the long-term allocation of energy away from height growth and towards weight growth. It seems possible that natural selection has shaped the way such tradeoffs are negotiated, much as it has shaped the tradeoffs between other life history demands. We might also predict differences in allocation tradeoffs when comparing populations, due to differing costs and benefits of increased height and weight due to differing local ecologies. For Shuar and most of South America, weight growth appears to be prioritized over height growth since stunting is reported to be prevalent, while wasting and underweight are uncommon.

Why should this be the case? We can think of several possible explanations, although at present cannot support one over the other. Climate likely plays a role in

shaping target body shapes (Bindon & Baker, 1997; Katzmarzyk & Leonard, 1998; Roberts, 1978; Ruff, 1993; Schell & Knutsen, 2002). In warm, dry climates, such as those found in parts of Africa, height growth may be prioritized over weight growth in order to achieve the long shape that best dissipates heat (Roberts, 1978; Ruff, 1993). In warm, humid environments, such as that found in the Amazon, the opposite may be true: a small body size may be beneficial since heat will be more difficult to dissipate, minimizing the benefits of height growth (Diamond, 1991; Schell & Knutsen, 2002; Stinson, 1990; Stinson, 2000). However, stunting is not limited to Amazonian populations; it is common across South American in diverse ecologies, including high altitude Andean and coastal populations (e.g. Stinson, 1980; Greksa et al., 1984; Leonard et al., 1990). Thus, it may be that for these populations it is the absence of selection for height that makes increased height "optional", rather than any positive selection for small body size. In populations with strong positive selection for height, such as the dry, hot savannas of East Africa, height may be "conserved", leading to increased relative prevalence of wasting instead of stunting.

A small body size may also be the result of life history tradeoffs between growth and reproduction—by terminating growth earlier, reproduction can begin earlier. Early termination of growth should be selected for in populations with high extrinsic mortality and short life expectancies (Migliano *et al.*, 2007; Walker *et al.,* 2006). Targeting energy into gain in weight rather than gain in height may also facilitate early reproduction due to early accumulation of the energy stores needed to reproduce. Such effects may be exaggerated by population history of resource stress and selection for so-called thrifty

genes, which prioritize energy stores and thus weight growth (Bindon & Baker, 1997). Finally, if Shuar weight is primarily lean body mass (muscle), it may be that arduous work effort is better supported by relatively muscular short bodies than tall thin ones, particularly in neo-tropical forest populations. For instance, Hill & Hurtado (1996) find an inverted U-shaped relationship (skewed toward the high end) between foraging returns and Ache male height.

While one or more of these factors may explain why Jivaroan children, in general, have slow height growth relative to weight growth, they are insufficient to explain the differences observed between Shuar, Shiwiar, and *colono* children, since these populations (with the possible exception of *colono*, whose ethnic history is less defined) are thought to be genetically similar with similar adaptive histories. To explain these differences multiple levels of explanation are needed. On an ultimate level, population adaptation to climate or resource availability may explain why height growth suffers more than weight growth under limiting conditions. These ultimate explanations still require proximate explanations for differences in resources between these populations, such as change in market integration.

Although this study benefits from its large sample sizes, future studies will need to address growth at both levels of explanation. Although our data suggests that market integration is negatively impacting growth in Shuar children, until data are available on diet, activity, pathogen exposure, and life histories, no conclusive statements can be made about the mechanisms causing these outcomes. Only with detailed, integrated data on all of these factors across a range of ecological conditions will we be able to parse out the

competing environmental and demographic demands affecting allocations of energy into weight gain, height gain, and maturation.

BRIDGE TO CHAPTER III

This chapter has examined the overall growth of Shuar children in comparison to other populations, and found that stunting is highly prevalent, but low weight-for-age and wasting are uncommon. Chapter III takes a deeper look at Shuar growth by examining variation in growth outcomes within the Shuar population. In Chapter III, I match the growth data used in this study with census data reporting household compositions. I examine the growth of children in 56 families living in 15 different Shuar villages and test specific predictions about the mechanisms through which market integration may be affecting Shuar growth. Namely, market integration may be affecting the relative ability of family members to contribute to pooled family resources. While examining the effects of market integration on growth, Chapter III also examines the hypothesis that humans are "cooperative breeders" who offset QQ trade-offs through broader alloparental investments and juvenile self-provisioning.

CHAPTER III

USE OF A POOLED RESOURCE MODEL TO ASSESS THE DIFFERENTIAL EFFECTS OF SHUAR FAMILY MEMBERS ON GROWTH ACROSS ECOLOGICAL CIRCUMSTANCES: IMPLICATIONS FOR COOPERATIVE BREEDING MODELS AND THE STUDY OF QUANTITY-QUALITY TRADE-OFFS IN HUMANS

This chapter is co-authored with Lawrence Sugiyama and Washington Tiwi. Lawrence Sugiyama was instrumental in organizing the field work and contributed to the theoretical development of this paper. Washington Tiwi organized the Shuar Federation survey that collected much of the data for this paper. All analyses, writing and figures were prepared by the author of this dissertation, and the age-summed modeling techniques used are the author's own invention.

INTRODUCTION

Life history theory (LHT) examines the trade-offs organisms face in the allocation of limited resources toward competing demands (Alexander, 1974; Charnov & Schaffer, 1973; Charnov, 1991; Charnov, 1993; Hill & Hurtado, 1996; Hill & Kaplan, 1999; Kaplan *et al.*, 2000; Lessels, 1991; MacArthur & Wilson, 1967; Schaffer, 1974; Stearns, 1976; Stearns, 1992). One such resource is parental investment, defined broadly as any investment into one offspring that decreases investment into another (Clutton-Brock, 1991; Trivers, 1972). Given that parental investment is a limited resource, one of the

most important trade-offs faced by parents is the trade-off between having many, low-quality offspring, or fewer, high-quality offspring (Williams, 1966). This trade-off was first recognized in avian clutch sizes and has since been investigated extensively in birds, reptiles and other animals (e.g., Lack, 1947; Monaghan & Nager, 1997; Uller *et al.*, 2006). However, only a handful of studies have tested for a quantity-quality trade-offs in humans, with sometimes mixed results. For example, !Kung foragers with average interbirth intervals of about 4 years have the highest number of surviving offspring, suggesting a decrease in quality with shorter interbirth intervals (Blurton Jones & Nicholas, 1986). In both a general Ecuadorian sample (Larrea & Kawachi, 2005) and among Shuar horticulturalists from Ecuador (Hagen *et al.*, 2006) children from families with more dependents have significantly poorer growth outcomes. In landless peasants in pre-industrial Finland, offspring contributions to maternal fitness decrease with maternal offspring production (Gillespie *et al.*, 2008), and among American children family size may decrease academic achievement, although being one of the last born in a very large family offsets this effect somewhat (Hanushek, 1992).

Other studies report mixed results. Borgerhoff Mulder (2000) found that Kipsigis women producing six or seven offspring maximized grandchildren, with grandchildren declining for women who produced more than seven. However, no effect was found for men. Similarly, Hill and Hurtado (1996) found that long-term fitness leveled off and possibly declined in Ache forager women from Paraguay when their lifetime completed fertility passed a certain point, but found no effect for men. In Israel, Angrist, et al (2006) found no evidence for a quantity-quality trade-off in educational attainment,

fertility, or earnings. In New Mexico, men with the most children also had the most grandchildren, although education and income were lower in high-fertility families (Kaplan *et al.*, 1995).

The failure in some cases to find evidence for a quantity-quality trade-off in humans might result from at least two important confounds. In part, failures to find trade-offs may be due to *phenotypic correlation*, whereby individuals with greater available energy allocate some of the additional energy to each branch of a trade-off. Where variance in energetic availability is significant, this can result in positive correlations between traits that are expected to trade off, instead of the expected negative correlations (Hagen *et al.,* 2006; Hill & Hurtado, 1996; McDade, 2003; Van Noordwijk & De Jong, 1986). In other words, families with more resources may have more children without reducing quality since resources per offspring remains constant. They may even have both more children and higher quality children than poorer families if there is sufficient energy to supply both needs. In captive populations of non-human animals, phentoypic correlation can be controlled for experimentally by holding resource availability constant. In humans and wild non-human populations this is obviously impossible, so statistical methods must be used to control for these correlations.

In order to control for phenotypic correlation in humans, it is important to ask what causes phenotypic variation in the first place. Some genetic variation in production ability, energy usage efficiency, and so on is expected. However, for most humans, social variables are likely to play a much greater role than genetic variability. These include socioeconomic and environmental conditions (such as degree of market

integration) and access to kinship networks that share resources and alloparental care (Hill & Hurtado, 1996). Attempts have been made to control for resource availability statistically, by including measures of wealth or productivity (e.g., Hagen *et al.*, 2006) or by dividing analyses categorically based on social or wealth status (e.g., Gillespie *et al.*, 2008). Which of these variables is most important varies depending on the specific context for a particular study. In an agricultural society, land ownership may be a critical variable (Gillespie *et al.*, 2008), whereas in small scale, egalitarian societies inter-household variation in wealth may be small, and it may therefore be kinship density or alloparental care that accounts for the greatest variation. This may be why many studies conducted in such societies find evidence for trade-offs, often without controlling for phenotypic correlation (Blurton Jones & Nicholas, 1986; Hagen *et al.*, 2006), whereas studies in Westernized, agricultural, or pastoral societies have more difficulty (Angrist *et al.*, 2006; Borgerhoff Mulder, 2000; Kaplan *et al.*, 1995).

Alloparenting and Cooperative Breeding

Alloparental investment is any investment given to an infant or juvenile by an individual who is not a biological parent. Alloparenting has been hypothesized to be a significant factor in the evolution of human life histories. Menopause and the substantial post-menopausal lifespan of females, for example, may have been selected for due to the contribution grandmothers make towards the survival and success of grand-offspring (Hawkes *et al.*, 1997; Hawkes *et al.*, 1998; Kramer *et al.*, 2009; Williams, 1966). In addition to direct alloparental investment, humans cooperate in other ways to raise

offspring, and so are sometimes referred to as *cooperative breeders*[1] (Hagen & Barrett, 2009; Hrdy, 2005; Hrdy, 2009; Kramer, 2005; Mace & Sear, 2005; Sugiyama & Chacon, 2005). For example, juveniles may self-provision or assist parents with simple chores which free parental time, resulting in higher parental production or ability to invest directly (Sugiyama & Chacon, 2005). Maya children, for example, produce about half of what they consume by age six and become net producers by age sixteen (Kramer, 2005).

Research to date has primarily focused on a few kin categories when examining direct and indirect effects of cooperators and alloparents on fitness-related outcomes such as growth, survival, and fertility (see Mace & Sear, 2005 for a review). Grandmothers, in particular, have been repeatedly found to have positive effects on grand-offspring (Gibson & Mace, 2005; Hawkes *et al.*, 1997; Mace & Sear, 2005; Sear *et al.*, 2000; Sear *et al.*, 2002). The effects of other kin are much more equivocal and/or variable across studies. Fathers, for example, may be incredibly important or relatively unimportant, depending on the context. In some hunter-gather societies, the meat obtained by male hunting is shared widely and not targeted directly toward the male's own offspring (Gurven, 2004; Hawkes & Bleige Bird, 2002) and the total calories produced by male hunting are sometimes significantly lower than the total produced by female foraging (Hill *et al.,* 1987; Marlowe, 2003). However, in some cases men may be able to target additional food towards their own households when such food is needed (Marlowe, 1999; Marlowe, 2003). Men may also invest differently depending on who else is investing;

[1] The exact use of this term is somewhat debated (Hagen & Barret, 2009). In animals it may be used to refer to species with sterile castes that assist reproduction, but in humans it is often used more broadly to refer to the often temporary delay or reduction in direct reproduction in order to assist kin.

among the Aka, children received more paternal care when families were living patrilocally, rather than matrilocally (Meehan, 2005). Finally, in some cases fathers may be important for protection from infanticide, rather than provisioning (Hill & Hurtado, 1996).

Siblings may also engage in a significant amount of alloparental care (Hagen & Barrett, 2009; Meehan, 2005), with many studies suggesting that adolescent sisters have the greatest impact on younger siblings (Bereczkei, 1998; Kramer, 2002; Sear *et al.*, 2002). However, among the Shuar, adolescent males have a positive effect on the growth of younger siblings, whereas adolescent females had a significant negative effect (Hagen & Barrett, 2009). They suggest that since they are preparing for reproduction, adolescent females may compete for food, whereas adolescent males who lack other reproductive opportunities invest their excess productivity into siblings. This may be similar to the situation among Pume foragers, where juvenile females appear to be buffered against the seasonal weight fluctuations experienced by older women (Kramer *et al.*, 2009).

While the variability in these findings might be taken to suggest that these classes of individuals were not important alloparents throughout human evolution, this interpretation would probably be incorrect, or at least an oversimplification. Clearly fathers are important in some contexts, as are adolescent siblings. A much more productive approach is to try and identify the variables affecting the importance of these supplementary caregivers, and then to use this information to hypothesize about 1) how evolution has shaped individuals to make decisions about when to alloparent and when not to (e.g., Sugiyama & Chacon, 2005) and 2) to determine how this pattern of variation

might have affected the evolution and context-dependent adjustment of other life history variables. One such approach, the ecological constraints model, suggests that individuals (particularly sexually mature siblings) should weigh the fitness benefits of alloparenting against the fitness benefits of establishing themselves as breeders, and that the costs and benefits of each option should depend on factors such as ability to alloparent, likelihood of breeding, and chance of survival (Emlen, 1982; Hagen & Barrett, 2009). More generally, we should expect alloparenting to follow the kin selection logic of Hamilton's Rule (Hamilton, 1964), but taking into consideration that costs and benefits will vary with context. For example, among the Aka, children living patrilocally received equivalent amounts of total investment, but from different individuals than those living patrilocally. Fathers invested more when the family lived patrilocally, while the mother's female kin invested most when the family lived matrilocally (Meehan, 2005). In the Aka case the context determines the effect individuals have, with context encompassing such things as the ability of different individuals to invest, the need for individuals to invest, and the opportunity costs of investment.

Market Integration and Life History Allocations

Previous studies have examined quantity-quality tradeoffs within single villages or across similar circumstances. While this allows for other confounding factors to be eliminated, it also prevents the examination of how life history tradeoffs are affected by changing environments and cultural milieus. Such effects are critical for understanding phenomena such as the demographic transition, which depends on life history allocations

shifting in response to new environmental cues. Of particular interest is how life history tradeoffs might be affected by changes in economy and subsistence.

Integration of indigenous groups with non-native society can lead to benefits such as education, economic opportunities, and access to health care. However, negative chronic health outcomes such as obesity and type-2 diabetes can also increase with market integration (Baker *et al.,* 1986; Friedlaender *et al.*, 1987; Huss-Ashmore *et al.*, 1992; Lindgarde *et al.*, 2004; Lindgarde *et al.*, 2006; Pavan *et al.*, 1999; Popkin, 2004; Shephard & Rode, 1996). For instance, Shuar living closer to markets have poorer growth than closely related but more traditionally living Shiwiar (Blackwell *et al.*, 2009). Many of these changes are linked to changes in diet, physical activity, and pathogen exposure.

These negative effects might proceed through a variety of causal pathways, but are likely related to changes in life history trade-offs. Changes in living arrangements, available resources, the costs of raising children, and opportunities for investment in other aspects of life are all expected to change alloparental and parental investment, including reproductive choices. Direct exposure to the norms of another culture can also affect preferences for number of offspring and expected offspring investment, or privilege competing goals, such as education or career. Less directly, individuals may observe the outcomes of other's decisions and reach conscious or subconscious conclusions about optimal solutions for the present environment (e.g. realizing that one's neighbor has too many children to care for). Changes in resource availability and risk exposure are also expected to affect life history tradeoffs, leading to changes in growth, reproductive timing, and total fertility.

The Present Study

In this study we use data on the growth of 129 Shuar children from 56 families (composed of 456 unique members), sampled from 15 different villages to 1) test for evidence of a quantity-quality trade-off using growth measures; 2) examine the effect of potential alloparents on growth; and 3) test the ecological constraints model of cooperative breeding by determining whether alloparental contributions vary with economic context. We utilize what might be thought of as a pooled energy model (Reiches *et al.*, 2009) in which a household is assumed to have a shared energy budget from which all household members draw and to which all household members contribute. We use this model as an analytical convenience—in reality most contributions do not go into a common pool, but travel between individual members. However, a pooled energy model allows us to set these interactions aside for the moment and examine the contributions of each member to the household as a whole (Reiches *et al.*, 2009).

Many studies have examined the effect of kin by dividing household members into age or sex graded categories (e.g. adolescents, juveniles, adult males, adult females, etc.), or have been forced to make assumptions *a priori* about which family members should be net producers and which consumers. While we replicate some of these strategies for comparability and hypothesis testing, our primary strategy is to use a pooled energy model to generate continuous age-functions for each sex describing the impact of household members on the growth of juveniles within the household. We test the following predictions: 1) younger juveniles will have negative effects on one another's growth due to competition for limited resources; 2) adult females will have positive

effects on the growth of their own children; and 3) the effects of other individuals, such and fathers and adolescents, will vary based on ecological constraints.

Ethnographic Context

Shuar are Amerindians from the Amazonas region of Ecuador, closely related to other groups such as the Achuar and Shiwiar who belong to what has been known as the Jivaroan language group (Descola, 1994; Descola, 1996; Harner, 1984; Sugiyama 2004). Traditionally, Shuar lived in scattered clusters of a few households, their economy based on horticulture, hunting, and fishing. Some Shuar, in the lowland region east of the Cutucu ridge that separates the Upano Valley from the "interior" Shuar, continue to practice hunting, fishing, and subsistence horticulture as well as small scale pastoralism in areas more isolated from road and river access. However, Shuar are experiencing very different effects of market integration across their territory. In the Upano Valley, Shuar are within walking distance to road access, hunting and fishing no longer appear to be critical parts of the economy, and subsistence garden sizes appear to be small. Shuar of the Upano valley are reported to have low protein diets and subsistence regime based largely on small field horticulture, minor animal husbandry, and wage labor.

Our previous work has shown that approximately 40% of Shuar children are stunted, and that Shuar are much more likely to be stunted than both the closely related Shiwiar and Achuar, as well as non-indigenous children living in the same area (Blackwell *et al.*, 2009). This comparison suggests that changes related to market integration may be negatively impacting Shuar growth.

METHODS

Data Sources

2005 School Childrens' Health Diagnostic. Shuar and *colono* data come from a 2005 health diagnostic conducted with the *Federacíon Interprovincial de Centros Shuar* (FICSH) and Hospital Pio XII in Sucúa, Ecuador. This data has been previously described in detail (Blackwell *et al.*, 2009). Briefly, the diagnostic includes 2,171 elementary-school age children (range = 1-17 years, mean = 8.3 ± 2.6), including 1,384 Shuar children (52% male, 48% female). Of these, 92.5% are from the Upano Valley, with the majority (65% of the total) living in Sucúa *parroquia*. The remaining 7.5% were from Yaupi *parroquia*, which lies across the Cutucu from the Upano Valley. In this document we refer to this data source as the Children's Health Diagnostic (CHD).

FISCH-FIPSE-FINAE Diagnostic of Shuar and Achuar Health Services and Situations. In 2005 and 2006 a census of Shuar and Achuar households was conducted through cooperation between three Shuar-Achuar organizations: the Federacíon Interprovincial de Centros Shuar (FICSH), the Federación Independiente del Pueblos Shuar (FIPSE), and the Federación Interprovincial de Nacionalidad Achuar del Ecuador (FINAE). The census recorded data such as access to health services and clean water by centro (village) and collected more specific data on household size and composition on a subset of households within each village, representing approximately one third of the households in the area. Some of this data has been previously reported (Jokisch and

McSweeney, 2006). For this study we use data on *centro* access, household composition, and household economic activities. Permission to use this data was obtained from FICSH and approved by the IRB at the University of Oregon. We refer to data as census data due to the nature of the information.

Data Matching

Individuals with data in both the census and CHD were matched on the basis of name, sex, *centro* (village), and age. In some instances ages were off by one year due to the census and children's health diagnostic being completed at different times. In total, 131 children from 56 families across 15 villages were unequivocally matched. Of these, three individuals were excluded. One had anthropometric data on only weight. Two had BMIs lower than 9.3, with NHANES z-scores of -12 and -15 and age and sex standardized residuals for BMI (see below) of -3.4 and -3.9. While it is theoretically possible that these individuals really do have BMIs this low, we checked their BMIs against the larger database of 1,384 Shuar and found that these three were two of the three lowest BMIs in the entire dataset. In addition, these two individuals had low BMIs not due to poor height and weight, but actually had above average age and sex standardized residuals for height (1.9 and 3.2) and below average residuals for weight (-2.8 and -1.6). We concluded that either the height or weight values for these individuals were likely in error and therefore excluded them from analysis.

The final sample includes 129 individuals from 56 families. Descriptive statistics for the 56 families are shown in Table 3.1, and the age distribution of all 456 members of

these families is shown in Figure 3.1. Unfortunately, although there are a few males in the sample as old as 70, the oldest female in the sample is 52, limiting our ability to examine the effects of older females on families. The age distribution is noticeably bimodal. Most families include two generations: parents and their offspring. The lack of individuals in their twenties and thirties may suggest that the sample is biased towards established households, rather than the households of young couples. It may also be due to the fact that these individuals are more likely to leave villages to pursue work in cities and towns.

Summary statistics for the 129 individual children on which we have anthropometric data are given in Table 3.2. The minimum age is five and the maximum sixteen. The sample is somewhat biased towards children from villages near the main road that runs the length of the Upano Valley (Figure 3.2).

Table 3.1. Summary of family characteristics

	Valid N	Minimum	Maximum	Mean	SD
Mother's Age	55	22.0	52.0	35.4	7.7
Father's Age	51	25.0	70.0	41.3	9.7
Parent's Age Difference (Father-Mother)	50	-5.0	20.0	5.4	5.4
Household Size	56	3	17	8.1	2.4
Females over 15	56	1	4	1.5	0.8
Males over 15	56	0	9	1.9	1.5
Head of Cattle	56	0	3	.50	.81
Pasture (ha)	56	0	50	12.35	16.26
Timber (Trees)	56	0	50	3.93	8.78
Cash Crops (ha)	56	0	3	.57	.85

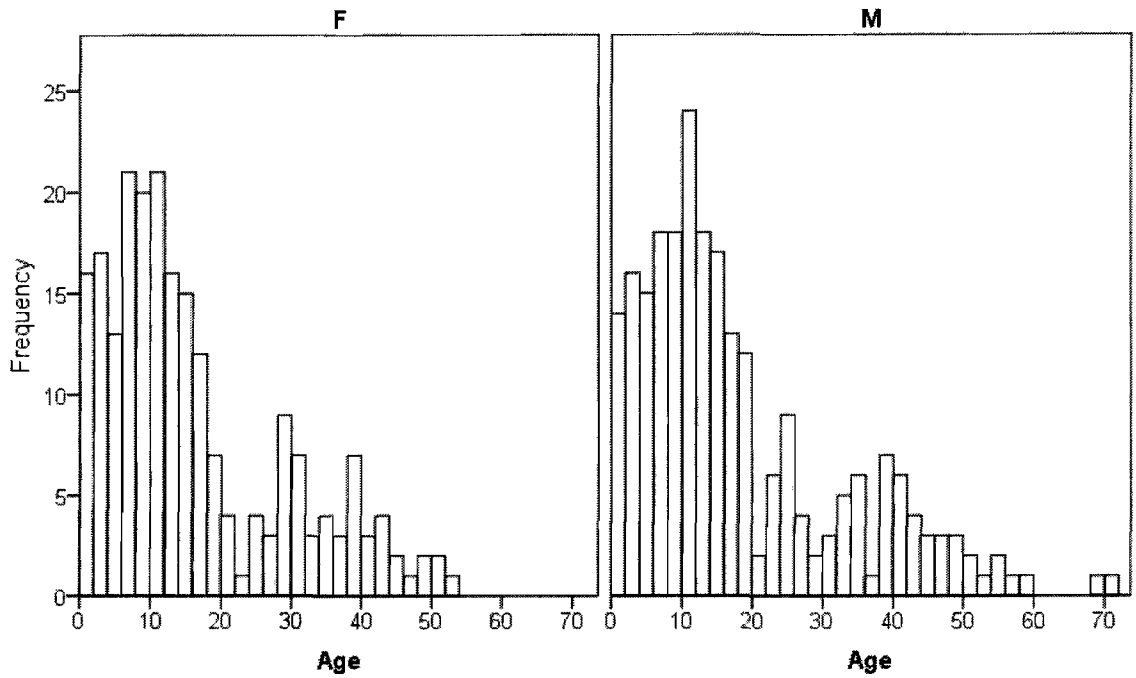

Figure 3.1. Age distribution of family members (n=456) for the 56 families in the sample.

Age and Sex Standardized Variables

To control for differences in anthropometric variables due to age and sex, age and sex standardized residuals were computed for height, weight, BMI, and number of caries using the full CHD data on 1,370 Shuar between the ages of 1 and 17. Residuals were computed based on the quadratic model $y = \beta_{1s} + \beta_{2s}*AGE + \beta_{3s}*AGE^2$, where *s* represents the sex of the individual. Model fits were very high for anthropometric measures (height $R^2 = 0.974$, weight $R^2=0.997$, BMI $R^2= 0.986$) but somewhat weaker for caries ($R^2 = 0.598$). Standardized residuals are referred to hereafter as HeightR, WeightR, BMIR, and CariesR. Mean anthropometric standardized residuals for the 129

individuals in this study were slightly below zero (Table 3.2) suggesting that the subsample used here has slightly poorer growth than the broader sample of Shuar on which the residuals are based.

Consumer to Producer Ratio

Hagen *et al.* (2006) used a consumer to producer ratio to investigate quantity-quality trade-offs in a Shuar village. *Consumers* were defined as all household members, and *Producers* were defined as women aged 15 or older, based on the argument that among the Shuar most nutritional calories are produced by women, whereas older males may work for cash or engage in hunting and fishing but contribute less consistently to

Table 3.2. Individual Sample Characteristics

	Males (N=67)				Females (N=62)			
	Min	**Max**	**Mean**	**SD**	**Min**	**Max**	**Mean**	**SD**
Age (years)	5.0	16.0	9.1	2.5	5.0	16.0	9.0	2.3
Birth Order	1.0	8.0	3.9	1.9	1.0	8.0	3.7	1.7
Weight (kg)	11.0	54.8	25.0	7.8	15.0	43.5	25.4	7.1
Height (cm)	97.0	157.5	122.0	13.3	101.0	146.0	121.3	11.9
BMI	9.8	22.1	16.4	2.1	12.2	22.2	16.9	2.0
# of Caries	0.0	14.0	4.6	3.4	0.0	16.0	4.3	3.4
WeightR	-2.53	2.78	-.36	.91	-1.97	1.67	-.32	.84
HeightR	-2.16	1.68	-.30	.94	-3.12	2.45	-.36	.98
BMIR	-2.82	2.10	-.30	.79	-1.93	1.62	-.11	.73
CariesR	-1.22	2.79	.09	.96	-1.27	3.60	.05	1.02
WAZ (NHANES)	-8.30	1.51	-1.45	1.48	-3.49	.81	-1.14	1.09
HAZ (NHANES)	-4.16	.61	-1.89	1.03	-4.19	1.13	-1.92	1.18
BAZ (HNANES)	-11.81	1.81	-.36	1.82	-3.17	1.34	.08	.85

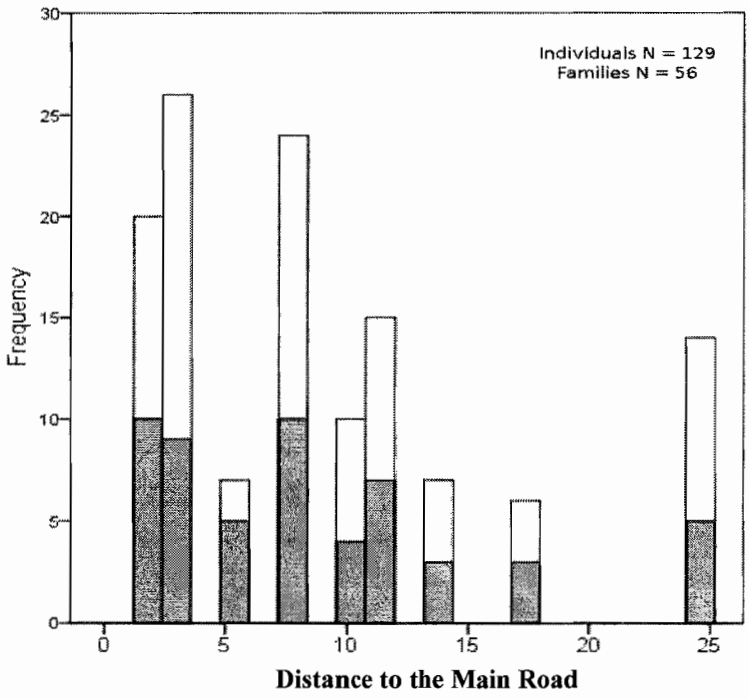

Figure 3.2. Histogram of sample size in terms of individuals (open bars) and families (grey bars) by village location relative to the main road

nutritional availability. Since we desired comparability with Hagen et al. we defined the consumer to producer ratio in the same way, referred to hereafter as F-CPR.

Analysis

For the 129 individuals matched between the two data sets, we used both mixed-effects models and univariate general linear models to investigate the factors contributing to household differences in HeightR, WeightR, BMIR, and CariesR. All analyses were done in SPSS 17.0 (SPSS Inc.). Mixed models were run using the Linear Mixed Models procedure with repeated subjects identified by household. Linear models were run with the univariate general linear model procedure. In some cases the linear regression

procedure with a backward parameter removal was used to remove covariates from the models. Further details are given with each analysis, below, including details of the pooled resource model.

RESULTS

Variation in Shuar Growth Variables across Villages and Households

A central assumption of this analysis is that Shuar growth will vary not just between individuals, but between household and communities. We first quantify this variation in order to estimate how much of the variance in growth and caries is attributable to these factors. We first entered household membership in an ordinary least squares (OLS) model. For the 56 families in this sample, household accounts for about 60% of the variation in HeightR (R^2=0.60, $F_{55,73}$ = 2.01, $p < .01$), BMIR (R^2=0.61, $F_{55,73}$ = 2.01, $p < .01$), and CariesR (R^2=0.65, $F_{55,73}$ = 2.50, $p < .01$), and about 50% of the variation in WeightR, although for weight the effect is not quite significant (R^2=0.53, $F_{55,73}$ = 1.50, p = .06). Note that household membership includes any variation due to differences between households, such as community membership. To parse community separately, we entered community into an OLS model. Village membership accounted for a little over 30% of the variation in HeightR (R^2=0.35, $F_{14,114}$ = 4.42, $p < .01$), WeightR (R^2=0.32, $F_{14,114}$ = 3.75, $p < .01$), BMIR (R^2=0.34, $F_{14,114}$ = 4.25, $p < .01$), and CariesR (R^2=0.31, $F_{14,114}$ = 3.71, $p < .01$).

These estimates from OLS are likely overestimates of the true variance due to community and household, since many of the families only have one or two children represented (thus a portion of the household variation is likely individual variation). To further examine the relative effects of individual, household, and community membership of variation, we used the variance components procedure in SPSS with a REML estimation model with community and household entered separately and together as random effects (Table 3.3). This procedure differs from the OLS procedure in that it assumes the households and communities are random samples of communities and households, rather than all the categories of interest. Thus, the variance components analysis attempts to generalize about the variation that would be expected in the full population. The procedure indicates that most of the variance is due to factors other than household and community. Controlling for community, household accounts for about 8% of the variance in Height and 10% of the variance in BMI, and about 23% of the

Table 3.3. Variance components due to Household and Community

	HeightR	**WeightR**	**BMIR**	**CariesR**
Household	.286	.170	.195	.384
Residual	.611	.580	.375	.584
Community	.234	.158	.140	.267
Residual	.657	.579	.426	.753
Household	.072	.001	.059	.222
Community	.215	.157	.123	.184
Residual	.599	.578	.380	.585
Total Variance	.907	.759	.582	.974

Three models for variance components in the dependent variables, HeightR, WeightR, BMIR, and CariesR. The first model includes only household, the second only community, and the third, both.

variance in Caries, but less than 1% of the variance in Weight. Community accounts for about 20% of the variance in each variable. Thus, when analyzing household level factors such as family composition, we should expect these factors to account for no more than the amount of variation accounted for here. Moreover, household differences appear to affect height and caries much more than they affect BMI and weight.

Consumer to Producer Ratio

We first replicated the method used by Hagen *et al.* (2006) to examine quantity-quality trade-offs in a Shuar village. Hagen and colleagues defined producers as females over age fifteen, and found that the ratio of consumers to producers was negatively associated with standardized residuals for height, weight, BMI and other anthropometric measures. We used both mixed effects models (MEM) and OLS models to examine the relationship between the ratio of consumers to females over fifteen (F-CPR) and the total number of consumers in the family (Table 3.4). We also tested for quadratic relationships. MEM and OLS models yielded similar parameters, but with lower significance values for the MEM model, as would be expected. By itself, number of consumers was not significantly related to any measure. F-CPR was significantly associated with declining HeightR (MEM: $\beta = -.11$, $p = .02$, Figure 3.3). No other significant linear or quadratic relationships were found.

If additional consumers are competing for resources, but additional producers are offsetting this condition, we would expect there to be a strong relationship between consumers and height when there are few producers, but little or no effect when there are

many producers. To parse out the relationship between Consumers, Producers, and height we ran a MEM with random household effects, Consumers, females over age fifteen (Producers), and a Consumers x Producers interaction. The original model parameters were non-significant, so we removed the main effect of Producers, which had the lowest F-statistic (in reference to Figure 3.4, this means that the slopes of all of the consumer lines have the same intercept). In the final model there is a significant negative main effect of Consumers (MEM: $\beta = -.16$, $p = .04$), but a significant positive interaction between Consumers and Producers (MEM: $\beta = .05$, $p = .01$), suggesting that each Producer decreases the negative effects of additional Consumers (Figure 3.4).

Table 3.4. Mixed effect and ordinary least squares (OLS) models for the effect of F-CPR and Consumers on standardized residuals for height, weight, BMI, and caries

	Mixed Effects Models					OLS Models		
	Fixed Effects		Random Effects					
Parameter	β	p	House hold	Residu al	AIC	β	R^2	p
HeightR								
Consumers	-.016	.742	.294	.612	351.95	-.012	.001	.767
F-CPR	-.114	.017	.244	.607	346.21	-.116	.065	.003
WeightR								
Consumers	-.031	.461	.171	.582	333.86	-.034	.007	.355
F-CPR	-.031	.470	.173	.581	333.82	-.031	.006	.398
BMIR								
Consumers	-.029	.448	.195	.376	292.25	-.037	.011	.245
F-CPR	.048	.219	.191	.375	291.23	.050	.019	.121
CariesR								
Consumers	.022	.662	.395	.584	355.88	.008	.000	.847
F-CPR	-.015	.769	.396	.584	355.90	-.005	.000	.908

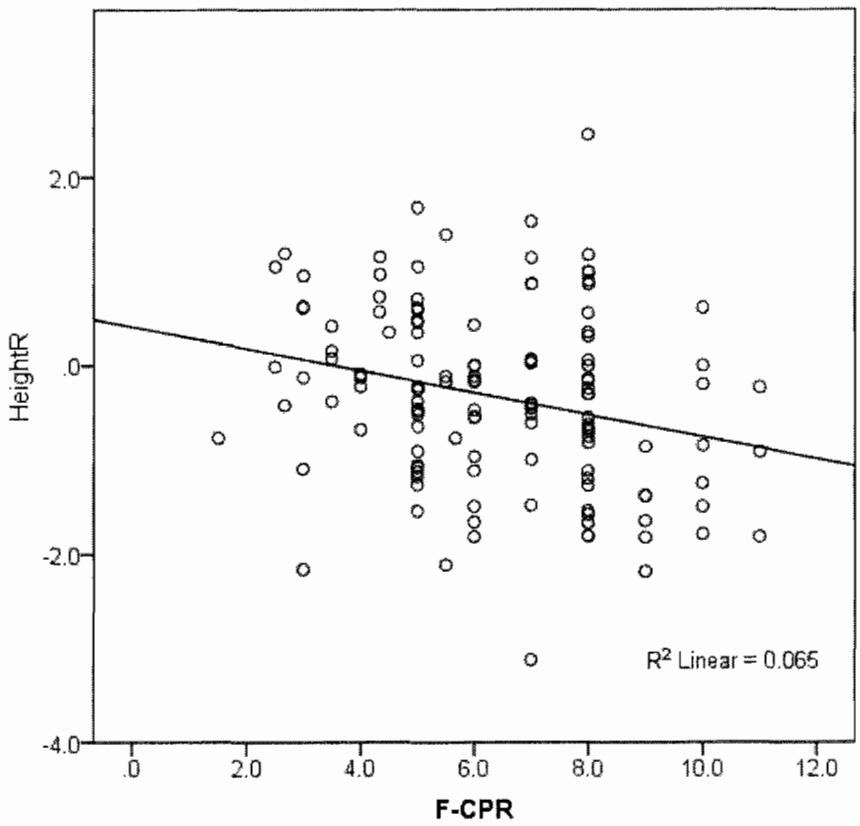

Figure 3.3. Relationship between F-CPR and HeightR

Economic Context – Geographical Location

One of our hypotheses is that the effect of alloparents will vary with opportunity costs and ability to invest, and that these should be a function of economic context. As a crude measure of economic context and market integration we first consider village location. All of the villages in this study are located in the Upano River Valley within a relatively small geographical area. However, within this area villages differ with ease of access to the main road, which is critical for things such as transporting lumber and cash crops and for regular access to markets and wage labor. Distance is not linearly related to

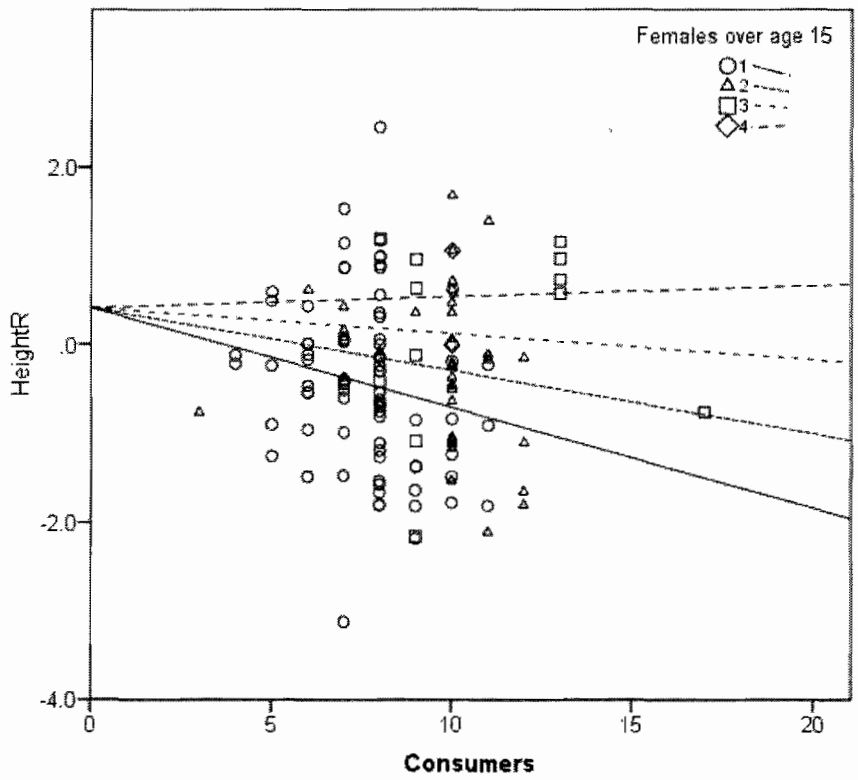

Figure 3.4. Consumers vs. HeightR for families with different numbers of females over age fifteen. Shapes represent families with one (circles), two (triangles), three (squares), or four (diamonds) females over age fifteen. Lines show the slope for each from a mixed effects model regressing Consumers (β = -.16, p= .04) and Consumers x Female Producers (β = .05, p= .01) on HeightR. Other model parameters: Intercept β = .41, p= .36; Random Effects: household σ^2 = .239, Residual σ^2 = .612. The main effect of Female Producers was removed from the model due to non-significance.

anthropometrics or caries (Table 3.5). However, HeightR (Figure 3.5) has a significant quadratic relationship with distance (MEM: Distance β = -.14, p< .01; Distance^2 β = .01, p< .01). CariesR also has a quadratic relationship to distance (MEM: Distance β = -.12, p= .03; Distance^2 β = .01, p= .02). The greatest heights and greatest number of caries are seen close to the main road or far from the main road. The lowest heights and lowest

caries are at intermediate distances. Neither WeightR nor BMIR were significantly predicted by distance.

We tested for interactions between F-CPR and distance (Table 3.6). For HeightR and WeightR, F-CPR interacts with distance to the main road such that F-CPR has the greatest negative effect at intermediate distances, but no effect close to the main road or in the most distant villages (Figure 3.6). This could mean that consumers do not have a negative effect in these areas (either because there is no cost or because some of them are net producers in these areas) or that females are less productive in these areas, so that it

Table 3.5. Effect of village distance from the main road on anthropometrics and caries

	Mixed Models					Linear Models		
	Fixed Effects		Random Effects					
Parameter	**β**	**p**	**House σ^2**	**Error σ^2**	**AIC**	**β**	**R^2**	**p**
Dependent: HeightR								
Distance (Linear)	-.014	.363	.287	.612	353.50	-.015	.012	.222
Distance (Quadratic)			.223	.612	356.95		.093	.002
Distance	-.143	.005				-.146		.000
Distance^2	.005	.007				.005		.001
Dependent: WeightR								
Distance (Linear)	-.018	.177	.165	.579	334.87	-.017	.019	.120
Distance (Quadratic)			.156	.579	343.61		.041	.071
Distance	-.080	.074				-.080		.039
Distance^2	.003	.143				.003		.090
Dependent: BMIR								
Distance (Linear)	-.012	.317	.197	.374	294.08	-.010	.008	.306
Distance (Quadratic)			.203	.374	305.12		.008	.591
Distance	-.010	.742				-.013		.708
Distance^2	.000	.967				.000		.930
Dependent: CariesR								
Distance (Linear)	.010	.536	.391	.584	357.94	.010	.005	.434
Distance (Quadratic)			.336	.582	362.59		.074	.008
Distance	-.116	.034				-.115		.008
Distance^2	.005	.017				.005		.003

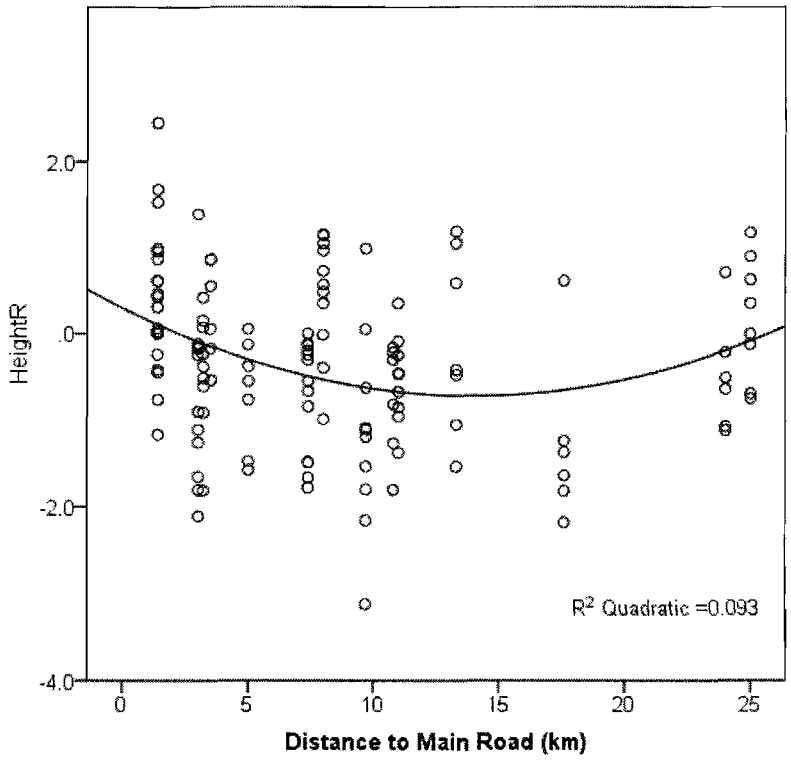

Figure 3.5. HeightR has a quadratic relationship with distance to the main road

takes a greater change in the number of females to have an effect on HeightR. To separate these effects, we ran a MEM with separate Consumer, Producer, and Consumer x Producer variables, as well as interactions between these terms and Distance. After removing non-significant terms in order of lowest F-statistic, the significant terms in the model include quadratic interactions between Distance and Consumers (Distance x Consumers: $\beta = -3.7 \times 10^{-2}$, $p < .01$; Distance^2 x Consumers: $\beta = 1.4 \times 10^{-3}$, $p < .01$) and three-way interactions between Distance, Consumers, and Producers (Distance x Consumers x Producers: $\beta = 1.1 \times 10^{-2}$, $p < .01$; Distance^2 x Consumers x Producers: β = -

$4.12x10^{-4}$, $p < .01$). The main effects of Consumers, Producers, and Distance were not significant. The model suggests that Consumers do indeed have the greatest negative effect at intermediate distances from the road, but that the mitigating effect of females is also greatest at intermediate distances (Figure 3.6). However, the two effects are not perfectly aligned as can be seen in Figure 3.7, which illustrates the effect on HeightR of Producers and Consumers and different distances. Even though the negative effect of additional consumers peaks at intermediate distances, it takes increasingly more consumers to fully offset the effect of more consumers.

Table 3.6. Interactions between F-CPR and distance to the main road

	HeightR		WeightR		CariesR	
Model A	**β**	**p**	**β**	**p**	**β**	**p**
Intercept	-.525	.427	-.917	.162	1.967	.012
F-CPR	.134	.182	.159	.109	-.243	.041
Distance	.215	.112	.208	.120	-.377	.018
Distance^2	-.008	.129	-.008	.105	.012	.050
F-CPR x Distance	-.058	.006	-.047	.024	.042	.083
F-CPR x Distance^2	.002	.010	.002	.029	-.001	.224
	σ^2		**σ^2**		**σ^2**	
Household	.132		.138		.303	
Residual	.604		.575		.584	
Model B	**β**	**p**	**β**	**p**	**β**	**p**
Intercept	.400	.023	.060	.728	1.331	.022
F-CPR	-	-	-	-	-.139	.088
Distance	-	-	-	-	-.205	.004
Distance^2	-	-	-	-	.005	.013
F-CPR x Distance	-.026	.000	-.013	.021	.014	.051
F-CPR x Distance^2	.001	.000	.0004	.060	-	-
	σ^2		**σ^2**		**σ^2**	
Household	.135		.143		.309	
Residual	.600		.574		.585	

Mixed effects models. For Model B, parameters from Model A were removed one at a time, least significant first, until all parameters were significant at the $p < .10$ level. BMIR is not shown since no parameters were significant

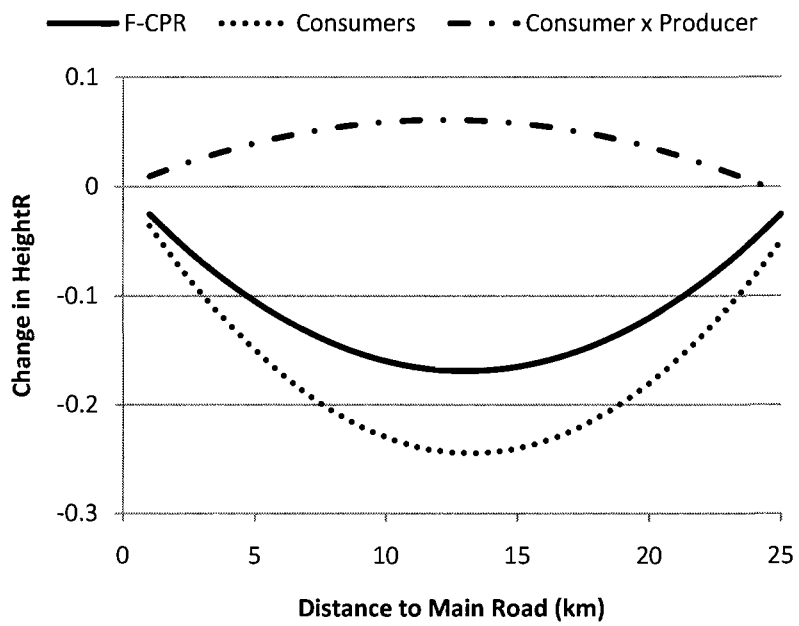

Figure 3.6. Effect of F-CPR, Consumers, and the Consumer x Producer interaction as a function of distance to the main road. The graph illustrates F-CPR from Model B in Table 3.6 and the effect of Consumers and the Consumer x Producer interaction from the MEM with the following parameters: Fixed Effects: Intercept $\beta = .38$, $p = .06$; Distance x Consumers $\beta = -3.7 \times 10^{-2}$, $p < .01$; Distance^2 x Consumers $\beta = 1.4 \times 10^{-3}$, $p < .01$; Distance x Consumers x Producers $\beta = 1.1 \times 10^{-2}$, $p < .01$, Distance^2 x Consumers x Producers $\beta = -4.12 \times 10^{-4}$, $p < .01$. Random Effects: household $\sigma^2 = .13$, Residual $\sigma^2 = .61$. The following terms were excluded from the model, in order of least significant first: Distance^2, Producers, Consumers, Distance, Consumers x Producers, Distance x Producers, Distance^2 x Producers

Other Economic Variables

In addition to geographical location, the census data includes household level economic variables that might relate to wealth and/or market integration. The variables include: number of cattle owned (Cattle), hectares of pasture land for cattle grazing (Pasture), hectares of land devoted to growing cash crops for sale (Cash Crops), and number of trees cut and sold in the last year (Timber). The dataset unfortunately does not

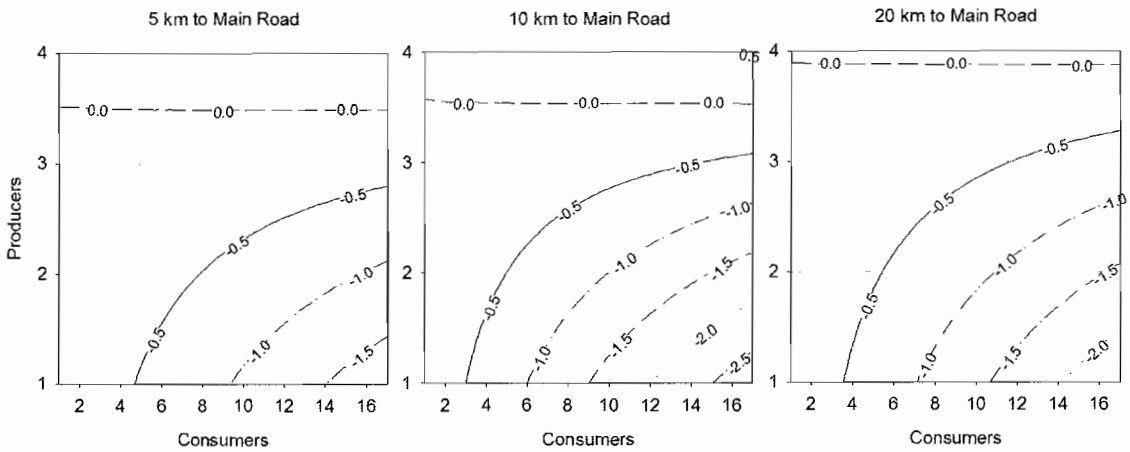

Figure 3.7. Interaction between Consumers and Producers (females over age 15) on HeightR as a function of village distance to the main road. The graph illustrates the MEM with the following parameters: Fixed Effects: Intercept $\beta = .38$, $p = .06$; Distance x Consumers $\beta = -3.7x10\text{-}2$, $p < .01$; Distance^2 x Consumers $\beta = 1.4x10\text{-}3$, $p < .01$; Distance x Consumers x Producers $\beta = 1.1x10\text{-}2$, $p < .01$, Distance^2 x Consumers x Producers $\beta = -4.1x10\text{-}4$, $p < .01$. Random Effects: household $\sigma 2 = .13$, Residual $\sigma 2 = .61$. The following terms were excluded from the model, in order of least significant first: Distance^2, Producers, Consumers, Distance, Consumers x Producers, Distance x Producers, Distance^2 x Producers

record hectares of vegetables grown for home consumption or other measures of household productivity unrelated to market participation. As one might expect, Cattle and Pasture are significantly correlated ($r=0.59$, $p < .01$, $n=56$), but the other economic variables are independent.

We first consider direct relationships between these wealth variables and anthropometric variables using mixed models to control for intra-household correlations. Cattle is not significantly associated with any anthropometric variable or CariesR. Considered separately, Pasture is associated with higher HeightR ($\beta = .013$, $p = .04$),

timber is positively associated with higher CariesR ($\beta = .030$, $p < .01$) and Cash Crops are associated with higher WeightR ($\beta = .214$, $p = .05$) and BMIR ($\beta = .198$, $p = .05$). Running multiple MEM with all four variables entered simultaneously changed these parameter values slightly, but did not change the direction of these effects nor which effects were significant.

If wealth is not an inherent difference between households, but is rather a product of having more producers in a family, then controlling for wealth should still effectively control for phenotypic correlations between traits expected to trade-off, but might interfere with the assessment of the impact of family members. We therefore tested for correlations between wealth variables and Consumers, Producers, Non-producers (individuals under age fifteen) and F-CPR for the 56 families. Pasture was significantly correlated with total number of Consumers ($r = .32$, $p = .02$), but also with females over age fifteen (Producers) ($r = .34$, $p = .01$), and males over age fifteen ($r = .31$, $p = .02$). Cattle was correlated only with males over age fifteen ($r = .27$, $p = .04$). Timber did not correlate with any variable. Cash Crops correlated negatively with F-CPR ($r = -.31$, $p = .02$) and there were a trends towards a positive correlation with adult females ($r = .21$, $p = .12$) and a negative correlation with Non-producers ($r = -.24$, $p = .08$). There were no other correlations that approached significance. Thus, these economic variables seem primarily to be a function of the adults in the family, with Pasture associated with adults of both sexes, Cattle with adult males, and Cash Crops with adult females living with few consumers under fifteen. (Perhaps these females can afford to sell crops, since the crops are not being eaten by children.)

We ran MEMs, first with F-CPR, Distance, and all four control variables (Table 3.7) and then with interaction terms between Distance and F-CPR (Table 3.8). For both we removed non-significant parameters one at a time until all parameters had p-values less than 0.10. Without the distance interaction terms, inclusion of control variables had little effect on the relationship between F-CPR and HeightR. Interestingly, controlling for Cash Crops results in a significant relationship between F-CPR and BMIR ($\beta = .76$, $p = .05$). On closer inspection, this is likely the result of the negative effect of F-CPR on

Table 3.7. Effect of F-CPR and distance to the main road on anthropometrics with wealth control variables

	HeightR		WeightR		BMIR		CariesR	
Model A	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**
Intercept	.740	.060	-.080	.827	-.642	.067	.581	.196
F-CPR	-.090	.047	.000	.999	.075	.065	-.023	.650
Distance	-.142	.003	-.077	.077	-.012	.770	-.113	.034
Distance^2	.006	.002	.003	.079	.000	.789	.004	.041
Cattle	-.204	.165	-.235	.094	-.147	.259	.017	.919
Pasture	.017	.016	.010	.123	.001	.841	.003	.695
Timber	-.012	.232	-.013	.178	-.008	.407	.027	.031
Cash Crops	.021	.854	.203	.071	.262	.014	-.135	.314
	σ^2		σ^2		σ^2		σ^2	
Household	.151		.122		.166		.294	
Residual	.605		.580		.377		.594	
Model B	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**
Intercept	.792	.031	-.045	.835	-.788	.005	.394	.111
F-CPR	-.097	.027	-	-	.076	.052	-	-
Distance	-.148	.002	-.082	.059	-	-	-.112	.029
Distance^2	.005	.003	.003	.109*	-	-	.004	.034
Cattle	-	-	-	-	-	-	-	-
Pasture	.011	.046	-	-	-	-	-	-
Timber	-	-	-	-	-	-	-	-
Cash Crops	-	-	.213	.048	.256	.013	-	-
	σ^2		σ^2		σ^2		σ^2	
Household	.142		.133		.158		.260	
Residual	.613		.578		.374		.596	

* Although the p-value of this term is greater than the 0.10 used for parameter removal, removing this term makes the effect of Distance on WeightR non-significant, so we have opted to present the model with these terms.

Table 3.8. Effect of F-CPR and distance to the main road on anthropometrics with wealth control variables and interactions between distance and F-CPR

	HeightR		WeightR		BMIR		CariesR	
Model A	β	p	β	p	β	p	β	p
Intercept	-.494	.496	-.791	.264	-.844	.209	1.932	.026
F-CPR	.107	.328	.113	.291	.107	.293	-.243	.063
Distance	.169	.243	.133	.344	.077	.562	-.384	.026
Distance^2	-.007	.203	-.007	.222	-.004	.381	.013	.054
F-CPR x Distance	-.051	.026	-.034	.118	-.015	.475	.044	.098
F-CPR x Distance^2	.002	.019	.002	.063	.001	.301	-.001	.184
Cattle	-.075	.627	-.167	.268	-.130	.371	-.137	.458
Pasture	.014	.048	.009	.178	.002	.793	.008	.323
Timber	-.009	.380	-.013	.191	-.010	.333	.019	.142
Cash Crops	.037	.742	.225	.044	.281	.009	-.120	.369
	σ^2		σ^2		σ^2		σ^2	
Household	0.115		0.107		0.167		0.277	
Residual	0.607		0.578		0.376		0.592	
Model B	β	p	β	p	β	p	β	p
Intercept	.233	.204	.060	.728	-.261	.024	.394	.111
F-CPR	-	-	-	-	-	-	-	-
Distance	-	-	-	-	-	-	-.112	.029
Distance^2	-	-	-	-	-.002	.065	.004	.034
F-CPR x Distance	-.025	<.001	-.013	.020	-	-	-	-
F-CPR x Distance^2	.001	<.001	.0004	.060	.0001	.095	-	-
Cattle	-	-	-	-	-	-	-	-
Pasture	.011	.036	-	-	-	-	-	-
Timber	-	-					.028	.019
Cash Crops	-	-	-	-	.242	.020	-	-
	σ^2		σ^2		σ^2		σ^2	
Household	.103		.143		.169		.260	
Residual	.604		.574		.372		.596	

height and the positive effect of Cash Crops on weight, rather than any change in weight associated with F-CPR .

In the model with Distance interaction terms (Table 3.8), controlling for wealth variables made essentially no difference for HeightR or WeightR. Although in the full model control variables made little difference in CariesR, in Model B, controlling for Timber made the effect of F-CPR non-significant. Unlike the model without control

variables where none of the parameters were significant with BMIR as the dependent variable, some variables did have $p < 0.10$ when controlling for Cash Crops. However, the parameters are not significant at the .05 level and have fairly limited effects, so the effect seems more likely due to chance.

A Pooled Resource Model for the Effect of Household Members

In examining the results for the interactions between Consumers, Producers and Distance, there are two issues raised. One is that the negative effect of consumers appears to change with distance. Although actual consumption levels are related to metabolic needs, they might change with distance if physical activity levels or pathogen exposure also change. A second possibility is that individuals other than females may be net producers in these areas. Among the Shuar, Hagen and Barrett (2009) have shown that adolescent males have a positive effect on siblings, at least in their study village. Both of these possibilities suggest that defining Producers and Consumers ahead of time is potentially problematic, and that improperly controlling for allomaternal investment might have a significant effect on the ability of studies to detect life history trade-offs.

Instead of using *a priori* categories of individuals to investigate allomothering and consumption levels, we developed a simple pooled energy model whereby household members contribute or deplete to the shared household energy pool based on their age and sex, and the energy pool, in turn, contributes to anthropometric variables. In practice we assume the energy pool as a theoretical concept and solve for the effect of household members on anthropometric variables directly. The pooled energy concept is useful since

we conceptualize the final effect on a household member as the sum of the effects of each individual member.

What we would ultimately like to know is the shape of the age function describing the effect of an individual on other household members. This function can be described as follows, where E_i is the effect of household member, i,:

$$\mathrm{E_i} = \sum_{p=0}^{n} \beta_{ps_i} A_i^p + e \qquad (1)$$

Eq. 1 is an n degree polynomial function of age, A, with function parameters (β) dependent on the sex of the individual, s, and with error e. Since the parameters differ with sex there are essentially two functions, one for males and one for females.

Ordinarily, we could use a simple linear regression to solve for the model parameters. However, in this case we do not know the dependent variable, E_i. Instead what we know are the standardized residuals for height, weight, BMI, and Caries, which we can assume are themselves a function of the total effect of all household members, E_{total}, on each outcome variable, respectively (e.g. HeightR = f(E$_{\text{total}}$). If we assume this function is approximately linear and express E_{total} in standardized height residual units then HeightR $\approx E_{total}$, and so on for the other standardized residuals. E_{total} in turn, equals the sum of the individual effects of the household's members ($i...j$) plus the effect not due to household members, α:

$$E_{total} = \alpha + \sum_{i=1}^{j} E_i \qquad (2)$$

Substituting Eq. 1 into Eq. 2:

$$E_{total} = \alpha + \sum_{i=1}^{j}\left(\sum_{p=0}^{n}\beta_{ps_i}A_i^p\right) + e_{total} \qquad (3)$$

Eq. 3 can be rearranged into equation 4, separating males ($m \ldots j_m$) and females ($m \ldots j_f$):

$$E_{total} = \alpha + \sum_{p=0}^{n}\left(\beta_{pf}\sum_{f=1}^{j_f}A_f^p\right) + \sum_{p=0}^{n}\left(\beta_{pm}\sum_{m=1}^{j_m}A_m^p\right) + e_{total} \qquad (4)$$

As Eq. 4 indicates, the model parameters ($\beta_{(p\ldots n)f}$, $\beta_{(p\ldots n)m}$), can be estimated using least squares regression, with the sums of household member ages, by sex, raised to the power p, as covariates (e.g. the sum of the ages of all females, the sum of the ages of all males, the sum of the squared ages of all females, the sum of the squared ages of all males, etc.) and standardized residuals as dependent values.

We calculated these sums for each household, up to the sum of ages to the fifth power for males and females ($\sum A^5$). Initially, we entered these sums as covariates in mixed effects models to estimate model parameters. However, the models fit tightly enough that the random effects of household were undefined. We therefore calculated household means for HeightR, WeightR, BMIR, and CariesR and used these as dependent values in a standard linear regression with a sample size of 56 households. We also used this same procedure to estimate the contributions of family members to the wealth variables of Cattle, Pasture, Timber, and Cash Crops. For all analyses, we used a backward parameter selection procedure to remove parameters in order of lowest partial correlation until we found the model with the highest adjusted R^2 value.

Economic Contributions as a Function of Age and Sex

Wealth variables work well for controlling for phenotypic correlations in quantity-quality tradeoff models. However, using them in a pooled resource model, where the effects of all family members are considered (rather than simply the effects of more offspring) presents additional complications. The single greatest complication is that these variables do not indicate access to resources independent of the work done by family members. As we noted above, Pasture appears to be related to the number of adults in a household, Cattle is correlated with males over age fifteen, and cash crops are associated with adult females living with few other household members. These variables can therefore be thought of as intermediates between household composition and anthropometric outcomes. If this is the case, then controlling for wealth variables will eliminate part of the effect attributable to the family member who is the source of the wealth. We therefore consider the effects of family members on wealth before considering the effects on anthropometrics.

We used the modeling procedure described above to estimate the effect of household members on wealth variables as a function of age and sex. The procedure yielded significant models for all variables except Cattle (Table 3.10). Model parameters are given in Table 3.9, and the final models are illustrated in Figure 3.8. Despite the fact that it is non-significant, the model for Cattle is almost identical to the model for Pasture (Figure 3.8). In both models females have little effect until age 35 or 40, at which point they have positive impact on both Pasture and Cattle. Males have small positive effects of Pasture and Cattle between age 10 and 50, followed by negative effects in old age.

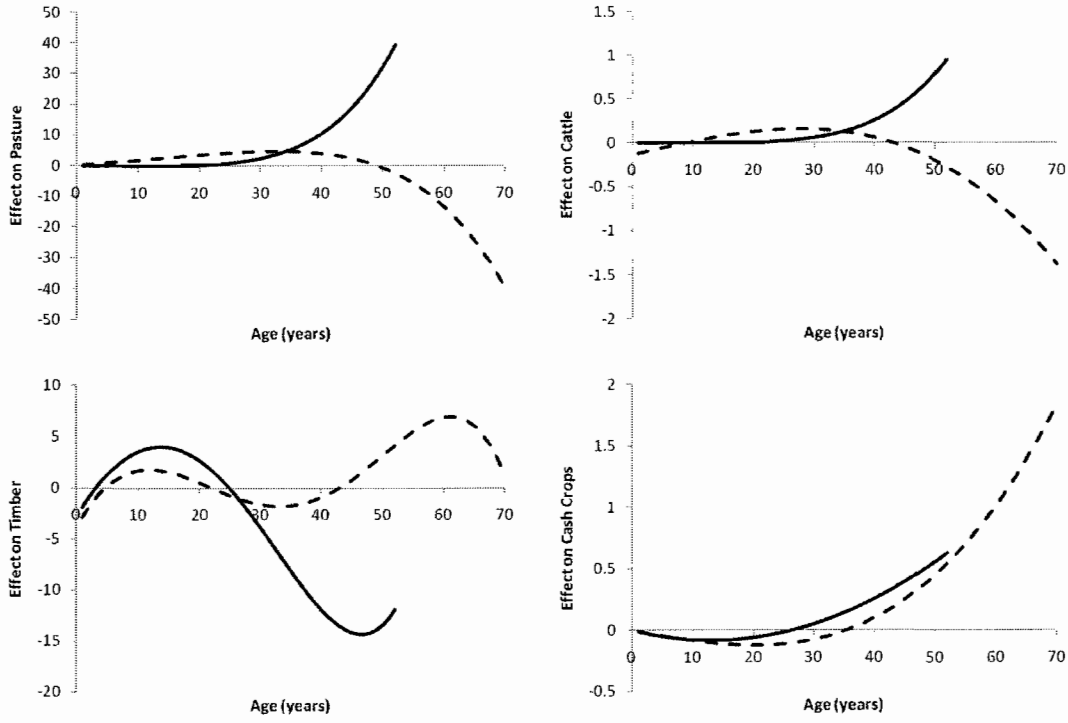

Figure 3.8. Wealth variables as a function of age and sex, as estimated using a backward regression procedure. Males are shown with dotted lines and females with solid lines. Note that the lines for females stop at age fifty-two since there are no older females in the sample. Model parameters are given in Table 3.9 and model statistics in Table 3.10.

The age and sex pattern for Timber is drastically different (Figure 3.8). Adolescents of both sexes have positive effects on Timber sales, but past age twenty-five the sexes diverge. Females over age twenty-five have strong negative associations with Timber sales. Males between twenty five and forty have small negative associations, but males older than age forty are associated with much greater sales of Timber, up until about age sixty.

Cash crops are associated with females over age thirty and males over the age of thirty-five, with total hectares increasing with age. Note that the difference between the

Table 3.9. Backward linear regression for the effect of a household member on wealth variables as a function of age and sex

	Pasture		Cattle		Timber		Crops	
	β	p	β	p	β	p	β	p
Intercept	-3.29	.439	2.70E-01	.301	3.38	.409	6.17E-01	.071
Females	-	-	-	-	-2.92	.128	-	-
Age	-	-	-	-	1.020	.002	-1.23E-02	.189
Age^2	-	-	-	-	-3.80E-02	.001	4.69E-04	.122
Age^3	-	-	-	-	-	-	-	-
Age^4	-	-	-	-	-	-	-	-
Age^5	1.03E-07	.002	2.49E-09	.177	1.07E-07	.054	-	-
Males	-	-	-1.33E-01	.236	-3.93E+00	.046	-	-
Age	1.79E-01	.001	1.60E-02	.041	1.13	.012	-8.93E-03	.012
Age^2	-	-	-	-	-6.87E-02	.014	-	-
Age^3	-	-	-6.92E-06	.040	1.20E-03	.014	7.17E-06	.004
Age^4	-	-	-	-	-	-	-	-
Age^5	-3.12E-08	.002	-	-	-8.85E-08	.020	-	-

Table 3.10. Backward regression model statistics with wealth variables as dependent variables

Model	R^2	adj. R^2	F	df (Reg.)	df (Res.)	p
Pasture	.290	.249	7.07	3	52	<.001
Cattle	.108	.038	1.54	4	51	.205
Timber	.385	.265	3.20	9	46	.004
Crops	.320	.266	5.99	4	51	<.001

female and male lines is approximately the mean age difference between married couples (Table 3.1).

Household Member Effects on Anthropometrics

Age and Sex. We next estimated models for the effects of household members on anthropometrics and caries. We ran two models, one without wealth control variables (Table 3.11) and one with control variables (Table 3.12). Wealth variables were allowed

Table 3.11. Backward linear regression for the effect of a household member on anthropometrics and CariesR as a function of age and sex, without wealth controls

	HeightR		WeightR		BMIR		CariesR	
	β	p	β	p	β	p	β	p
Females	-.186	.073	-	-	-	-	-	-
Age	.013	.051	-.015	.050	-.029	.006	-	-
Age^2	-	-	-	-	-	-	-	-
Age^3	-	-	.000	.132	.000	.145	-	-
Age^4	-	-	-	-	-	-	-	-
Age^5	-	-	-	-	.000	.267	-	-
Males	-	-	-	-	-	-	-	-
Age	-	-	-.022	.090	-.033	.023	.004	.235
Age^2	-	-	.001	.086	.002	.026	-	-
Age^3	-	-	.000	.128	.000	.074	-	-
Age^4	-	-	-	-	-	-	-	-
Age^5	-	-	-	-	-	-	-	-
Intercept	.063	.894	.425	.258	.282	.418	-.031	.943
Distance	-.104	.049	-.092	.050			-.073	.316
Distance^2	.004	.067	.003	.100			.004	.166

Table 3.12. Backward linear regression for the effect of a household member on anthropometrics and CariesR as a function of age and sex, with wealth controls

	HeightR		WeightR		BMIR		CariesR	
	β	p	β	p	β	p	β	p
Females	-.251	.049	-	-	-	-	-.181	.058
Age	.019	.097	-	-	-	-	-	-
Age^2	-	-	-.002	.044	-.003	.004	-	-
Age^3	-	-	.000	.083	.000	.012	.000	.049
Age^4	-	-	-	-	-	-	-	-
Age^5	.000	.117	.000	.200	.000	.052	-	-
Males	-	-	-	-	-	-	-	-
Age	-	-	-.017	.132	-.047	.030	-	-
Age^2	-	-	.001	.077	.004	.036	.001	.061
Age^3	-	-	.000	.102	.000	.082	.000	.045
Age^4	-	-	-	-	-	-	-	-
Age^5	-	-	-	-	.000	.207	-	-
Intercept	-.024	.948	.169	.639	.260	.454	-.012	.978
Distance	-.086	.086	-.081	.082	-	-	-	-
Distance^2	.003	.091	.003	.105	-	-	-	-
Cattle	-.356	.020	-.208	.071	-.225	.083	-	-
Pasture	.022	.006	-	-	-	-	-.015	.120
Timber	-	-	-	-	-	-	.061	.001
Cash Crops	.294	.024	.330	.009	.218	.121	.294	.024

to exit the model in the same way as the other parameters. The final model statistics are given in table Table 3.13 and are illustrated graphically in Figure 3.9. Models with wealth control variables had much higher R^2 values than those without (Table 3.13). Moreover, these models were significant, whereas the models without wealth controls were not.

Regardless of whether controls are included, males have no significant effect on HeightR, whereas females have increasingly positive effects with age. In the model with controls, this effect declines significantly after age forty and becomes negative for females older than about forty-five. In this model, Cattle has a significant negative effect on HeightR, but this is countered by a positive effect from Pasture. Cash Crops also have a significant positive effect. The difference between these two models and the fact that older females are also associated with Cash Crops and Pasture (Figure 3.8) suggests that controlling for these factors removes the positive effect of older females from the model. The models for WeightR and BMIR mirror each other closely. In these models males clearly have the greatest effect. Males begin to have a positive effect at age twenty, which increases until around age fifty and then declines. Females appear to have a negative effect on WeightR and BMIR until age forty or so, and even then they appear to have a neutral or slightly positive effect for only a few years. For CariesR, significant effects are only seen when controlling for wealth variables. In this model, females over about age 25 increase the number of caries, whereas males have a small positive effect under age 40, after which they have a negative effect on CariesR. Note that in this

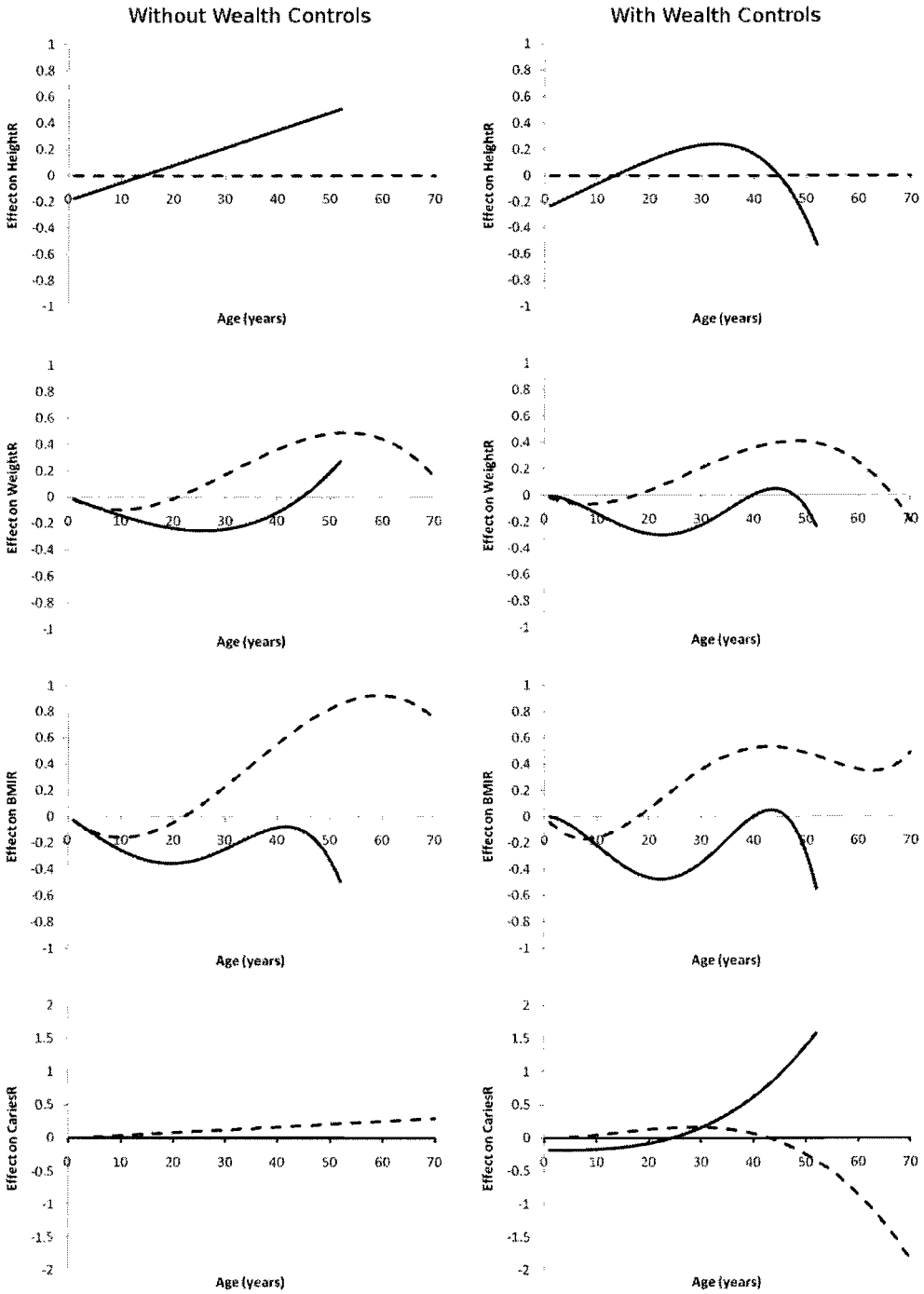

Figure 3.9. Effect of family members on HeightR, WeightR, and CariesR. Y-axis is the age of the family member. Males are shown with dotted lines and females with solid lines. Note that the lines for females stop at age fifty-two since there are no older females in the sample. Model parameters are given in Tables 3.11 and 3.12 and model statistics in Table 3.13.

Table 3.13. Fit statistics for models without Distance interaction terms

	R^2	adj. R2	F	df (Reg.)	df (Res.)	p
No Controls						
HeightR	.162	.096	2.46	4	51	.057
WeightR	.184	.065	1.54	7	48	.175
BMIR	.192	.093	1.94	6	49	.092
CariesR	.073	.020	1.37	3	52	.263
With Controls						
HeightR	.355	.245	3.23	8	47	.005
WeightR	.328	.179	2.20	10	45	.036
BMIR	.289	.150	2.08	9	46	.051
CariesR	.247	.155	2.68	6	49	.025

model, both Timber and Cash Crops increase caries, suggesting that caries are related to market activities

Distance to the Main Road. Since we had previously found that F-CPR, Consumers, and Producers interact with distance from the main road (Distance), we next added interaction terms to Eq. 5 to model the quadratic effect of village distance from the main road, *D,* on the models parameters:

$$E_{total} = \alpha + \sum_{p=0}^{n}\left(\left(\beta_{pf} + \beta_{p.2f}D + \beta_{p.3f}D^2\right)\sum_{f=1}^{j_f} A_f^p\right) + \sum_{p=0}^{n}\left(\left(\beta_{pm} + \beta_{p.2m}D + \beta_{p.3m}D^2\right)\sum_{m=1}^{jm} A_m^p\right) + e_{total} \qquad (5)$$

As before, we used a backward linear regression with polynomial terms up to the sum of Age^5 and removed non-significant terms from the models one at a time in order of lowest partial correlation until we found the model with the highest adjusted R^2. Models were

Table 3.14. Fit statistics for models with Distance interaction terms

	R^2	adj. R^2	F	df (Reg.)	df (Res.)	p
No Controls						
HeightR	.634	.441	3.29	19	36	.001
WeightR	.607	.416	3.18	18	37	.001
BMIR	.484	.272	2.29	16	39	.018
CariesR	.506	.303	2.49	16	39	.010
With Controls						
HeightR	.736	.560	4.18	22	33	<.001
WeightR	.662	.437	2.94	22	33	.002
BMIR	.531	.303	2.33	18	37	.014
CariesR	.595	.364	2.57	20	35	.007

run with standardized residuals for height, weight, BMI, and caries as the dependent variables, and were run twice, once with and once without the wealth control variables. All models were highly significant (Table 3.14). Final model parameters are shown in Tables 3.15 and 3.16.

The model for HeightR is illustrated in Figure 3.10. Unlike the main effect models in Figure 3.9, the model suggests that males of some ages and in certain areas do have a positive effect on height. Namely, in areas close to town, adolescent and adult males have a positive effect that increases with age, and in the most distant areas males over age 25 (not controlling for wealth) or age 35 (controlling for wealth) have a positive effect, but adolescents do not. For intermediate villages males have solid negative effects that increase with age. Interestingly, male juveniles appear to have a positive effect in intermediate villages, but this effect disappears once wealth controls are included, suggesting that the uncontrolled effect may be due to phenotypic correlation. Female

juveniles have negative effects throughout, although in villages close to the main road they begin to have positive effects around age five. Adolescent females also have positive effects in these villages, though they do not elsewhere. Adult females have the greatest effect in intermediate villages, although this effect declines in villages close to the road and most distant, such that females over age 35 or so actually have a negative effect in these villages.

The graphs for WeightR show a similar general pattern to the graphs for HeightR, except that the range for which males have a positive effect is somewhat greater and the effect of female somewhat decreased. Males again have a positive effect in the most distant and least distant villages. In the villages close to the main road, the effect is limited to males age fifteen to sixty or sixty-five. In the most distant villages males begin to have a positive effect on WeightR around age ten. Females age about 20 to 40 have positive effects on weight in all villages except those nearest to the main road. Females in the closest villages have positive effects after age 45, although the sample here is limited. Depending on whether wealth variables are controlled for, adolescent females also have positive effects in these villages. Juvenile males again have consistent negative effects regardless of distance. Juvenile females also have consistent negative effects when controlling for phenotypic correlations with wealth variables.

The graphs for BMIR (Figure 3.12) show a pattern that is quite different from the HeightR and WeightR patterns. BMI is unique in that BMI represents an interaction between height and weight, so interpreting changes in BMI can be somewhat more difficult, since a decrease in height that is not accompanied by a decrease in weight

causes a positive effect on BMI. Consistent with Figure 3.9, and with their greater impact on weight than height, males have the greatest positive impact on BMIR. For the nearest villages, the positive impact ranges from about age 20 to age 60. In the distant villages, adolescents over age 10 or so also have a positive effect. Although there are no individuals over age fifty-two in the distant villages, in the villages near to the road males over age sixty have clear negative effects. Females mostly have slight negative effects on BMIR, likely due to their greater impact on height than on weight, rather than due to negative effects on either. The exception may be the females over age forty in the closer villages, who have a positive effect on weight and BMI, but not height. Juveniles generally have negative effects on BMI as well, except that controlling for wealth variables, juvenile males in intermediate villages and juvenile females in near villages have positive effects on BMI. This may again be due to greater negative effects on height than on weight.

Juveniles do, however, have significant positive effects on CariesR, especially in intermediate villages (Figure 3.13). Males also increase CariesR. It is not surprising that males increase caries, since it is mostly males who work for cash and purchase processed goods which may be related to increased caries. However, the increase associated with juveniles is somewhat surprising and suggests that competition for resources may affect caries, much as it affects height and weight. The exact cause, however, cannot be ascertained based on the data available for this study.

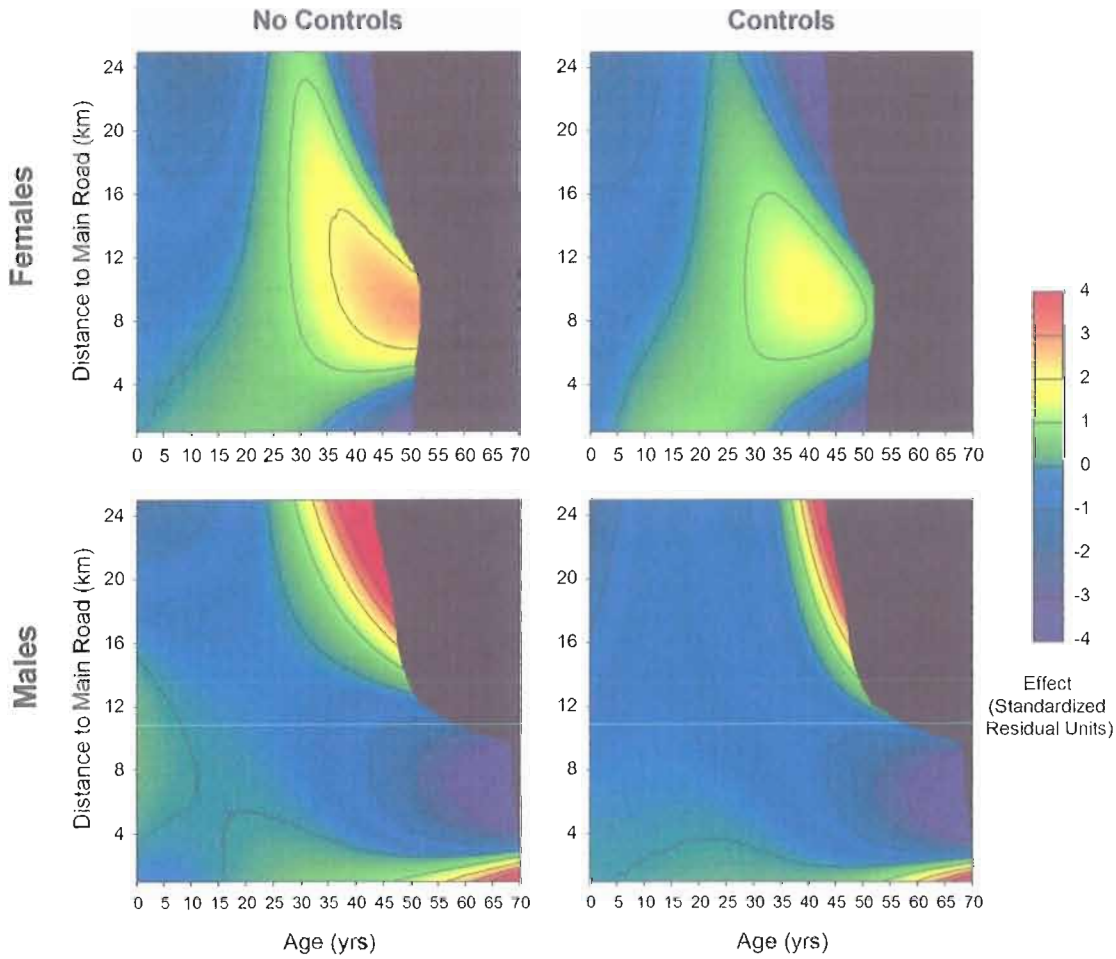

Figure 3.10. Household member effect on HeightR as a function of age, distance to the main road, and sex. Model parameters are shown in Table 3.15 and Table 3.16, and model statistics in Table 3.14. Areas for which there are no samples are masked in black.

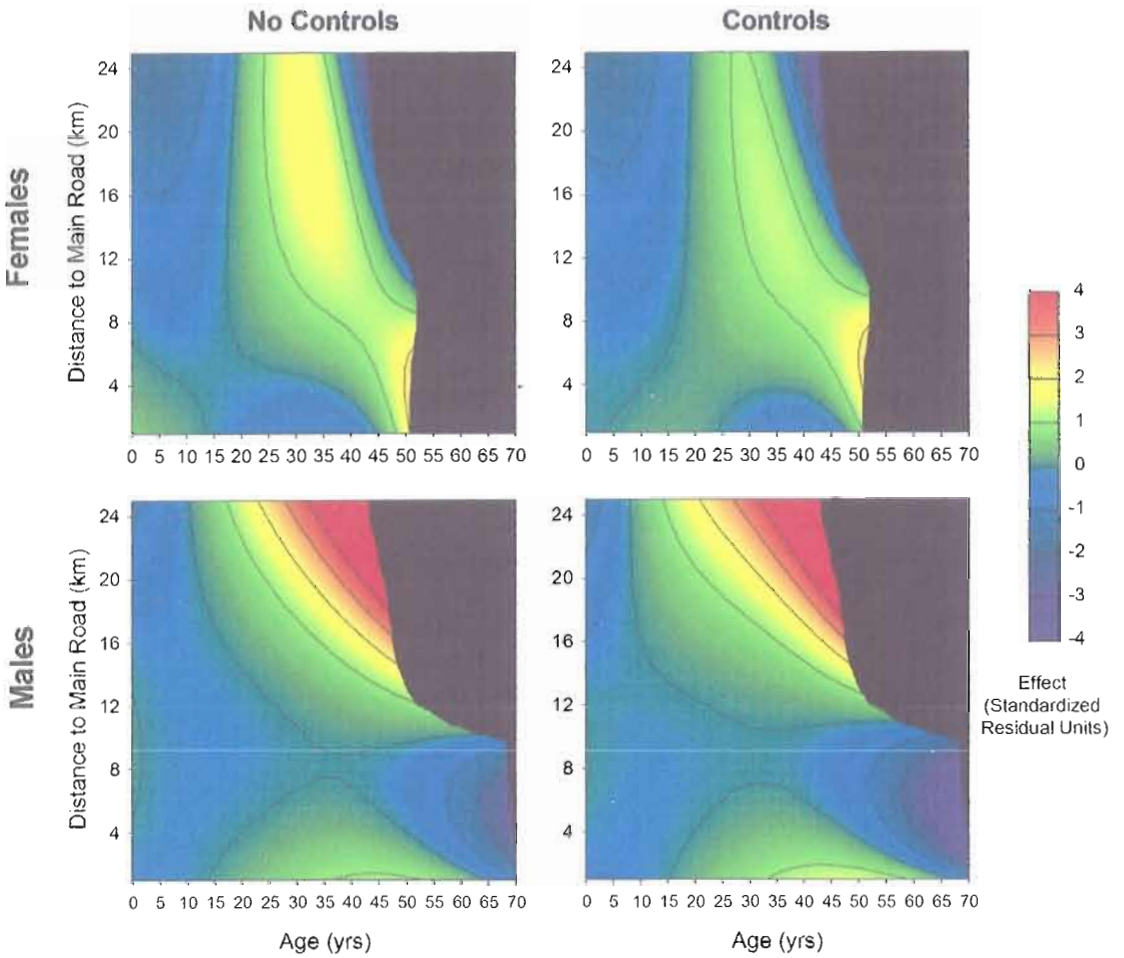

Figure 3.11. Household member effect on WeightR as a function of age, distance to the main road, and sex. Model parameters are shown in Table 3.15 and Table 3.16, and model statistics in Table 3.14. Areas for which there are no samples are masked in black.

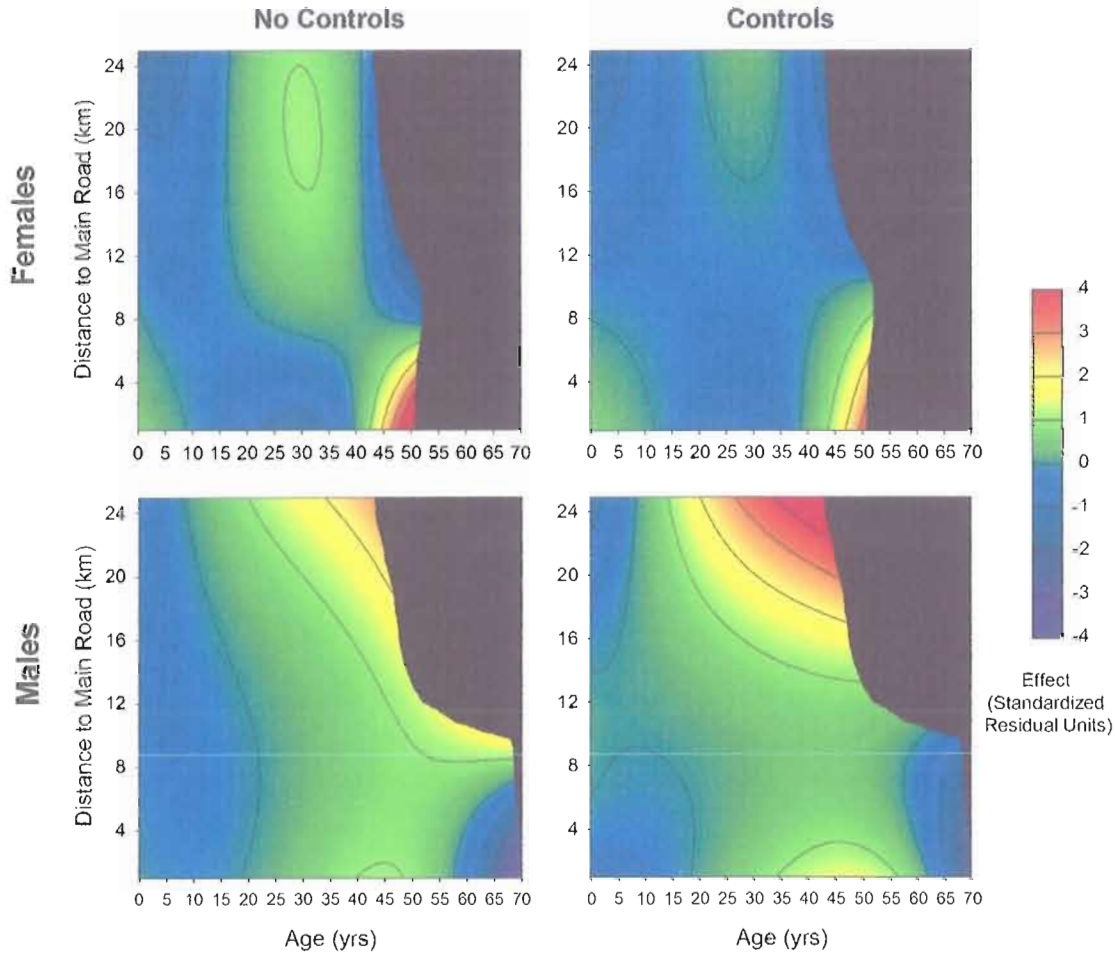

Figure 3.12. Household member effect on BMIR as a function of age, distance to the main road, and sex.

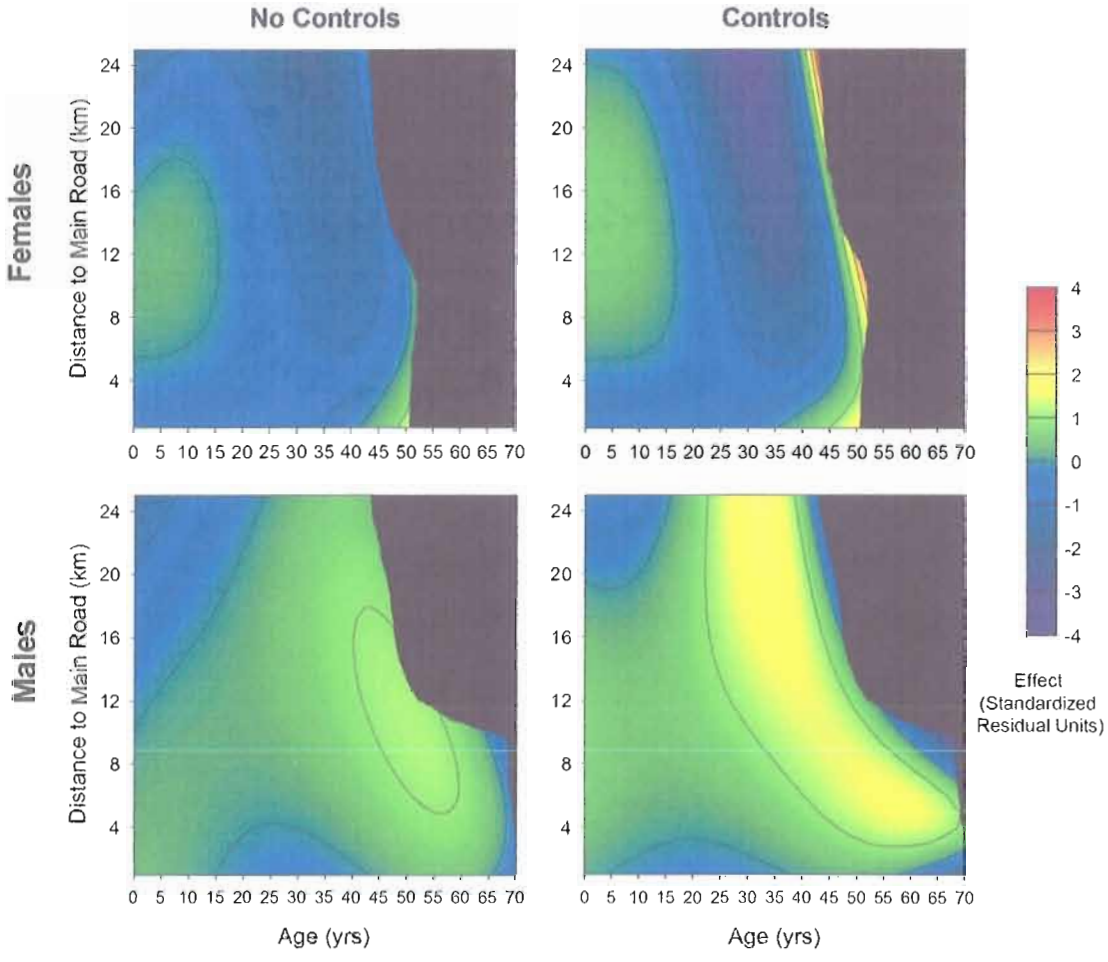

Figure 3.13. Household member effect on CariesR as a function of age, distance to the main road, and sex.

Table 3.15. Backward linear regression for the effect of a household member on anthropometrics and CariesR as a function of age, sex, and distance to the main road

Parameter	HeightR β	p	WeightR β	p
Intercept	2.74E-01	.719	-1.81E-01	.537
Dist	-3.14E-01	.163	-	-
Distance^2	2.37E-02	.095	-	-
Females				
$B_{0.1f}$ (n_f)	-	-	6.10E-01	.003
$B_{0.12f}$ (n_f x Distance)	-4.17E-02	.016	-9.08E-02	<.001
$B_{0.3f}$ (n_f x Distance^2)	-	-	-	-
$\beta_{1.1f}$ (Age)	2.88E-02	.007	-3.77E-02	.046
$\beta_{1.2f}$ (Age x Distance)	-	-	-	-
$\beta_{1.3f}$ (Age x Distance^2)	-2.65E-04	.012	-1.04E-04	.110
$\beta_{2.1f}$ (Age^2)	-	-	-	-
$\beta_{2.2f}$ (Age^2 x Distance)	-	-	4.58E-04	<.001
$\beta_{2.3f}$ (Age^2 x Distance^2)	-	-	-	-
$\beta_{3.1f}$ (Age^3)	-	-	-4.72E-05	.105
$\beta_{3.2f}$ (Age^3 x Distance)	-	-	-	-
$\beta_{3.3f}$ (Age^3 x Distance^2)	7.50E-07	.003	-	-
$\beta_{4.1f}$ (Age^4)	-	-	-	-
$\beta_{4.2f}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3f}$ (Age^4 x Distance^2)	-	-	-	-
$\beta_{5.1f}$ (Age^5)	-3.07E-08	<.001	2.73E-08	.044
$\beta_{5.2f}$ (Age^5 x Distance)	8.24E-09	<.001	-2.21E-09	.055
$\beta_{5.3f}$ (Age^5 x Distance^2)	-7.20E-10	<.001	-1.29E-10	.007
Males				
$B_{0.1m}$ (n_m)	-4.48E-01	.043	-3.22E-01	.054
$B_{0.12m}$ (n_m x Distance)	1.59E-01	.011	8.92E-02	.061
$B_{0.13m}$ (n_m x Distance^2)	-8.56E-03	.004	-4.97E-03	.024
$\beta_{1.1m}$ (Age)	-	-	-	-
$\beta_{1.2m}$ (Age x Distance)	-8.95E-03	.020	-1.04E-02	.003
$\beta_{1.3m}$ (Age x Distance^2)	4.02E-04	.043	5.64E-04	.002
$\beta_{2.1m}$ (Age^2)	2.49E-03	.025	2.39E-03	.006
$\beta_{2.2m}$ (Age^2 x Distance)	-	-	-	-
$\beta_{2.3m}$ (Age^2 x Distance^2)	-	-	-	-
$\beta_{3.1m}$ (Age^3)	-5.42E-05	.026	-3.22E-05	.033
$\beta_{3.2m}$ (Age^3 x Distance)	-	-	-	-
$\beta_{3.3m}$ (Age^3 x Distance^2)	-	-	-	-
$\beta_{4.1m}$ (Age^4)	-	-	-	-
$\beta_{4.2m}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3m}$ (Age^4 x Distance^2)	-	-	-	-
$\beta_{5.1m}$ (Age^5)	1.04E-08	<.001	-	-
$\beta_{5.2m}$ (Age^5 x Distance)	-2.46E-09	<.001	-4.83E-10	.221
$\beta_{5.3m}$ (Age^5 x Distance^2)	1.83E-10	.001	6.16E-11	.053

Table 3.15. (continued)

Parameter	BMIR β	p	CariesR β	p
Intercept	2.02E-01	.589	2.78	.010
Dist	-	-	-8.22E-01	.001
Distance^2	-	-	4.37E-02	.001
Females				
$B_{0.1f}$ (n_f)	6.99E-01	.001	-8.23E-01	.003
$B_{0.12f}$ (n_f x Distance)	-8.13E-02	<.001	2.01E-01	<.001
$B_{0.3f}$ (n_f x Distance^2)	-	-	-9.44E-03	.001
$\beta_{1.1f}$ (Age)	-7.24E-02	.002	-	-
$\beta_{1.2f}$ (Age x Distance)	-	-	-	-
$\beta_{1.3f}$ (Age x Distance^2)	-	-	2.14E-04	.133
$\beta_{2.1f}$ (Age^2)	6.02E-04	.002		
$\beta_{2.2f}$ (Age^2 x Distance)	-	-	-2.49E-04	.017
$\beta_{2.3f}$ (Age^2 x Distance^2)	-	-	-	-
$\beta_{3.1f}$ (Age^3)	-4.60E-05	.166	-	-
$\beta_{3.2f}$ (Age^3 x Distance)	-	-	-	-
$\beta_{3.3f}$ (Age^3 x Distance^2)	-5.24E-07	.049	-	-
$\beta_{4.1f}$ (Age^4)	-	-	-	-
$\beta_{4.2f}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3f}$ (Age^4 x Distance^2)	-	-	-	-
$\beta_{5.1f}$ (Age^5)	5.09E-08	.010	8.21E-09	.053
$\beta_{5.2f}$ (Age^5 x Distance)	-8.42E-09	.002	-	-
$\beta_{5.3f}$ (Age^5 x Distance^2)	3.21E-10	.047	6.89E-11	.093
Males				
$B_{0.1m}$ (n_m)	-	-	3.26E-01	.029
$B_{0.12m}$ (n_m x Distance)	-2.68E-02	.067	-	-
$B_{0.13m}$ (n_m x Distance^2)	-	-	-3.18E-03	.022
$\beta_{1.1m}$ (Age)	-3.63E-02	.040	-	-
$\beta_{1.2m}$ (Age x Distance)	-	-	4.08E-03	.008
$\beta_{1.3m}$ (Age x Distance^2)	1.67E-04	.008	-	-
$\beta_{2.1m}$ (Age^2)	2.11E-03	.016	-2.85E-03	.011
$\beta_{2.2m}$ (Age^2 x Distance)	-	-	-	-
$\beta_{2.3m}$ (Age^2 x Distance^2)	-	-	-	-
$\beta_{3.1m}$ (Age^3)	-	-	7.41E-05	.011
$\beta_{3.2m}$ (Age^3 x Distance)	-2.92E-06	.098	-	-
$\beta_{3.3m}$ (Age^3 x Distance^2)	-	-	-	-
$\beta_{4.1m}$ (Age^4)	-	-	-	-
$\beta_{4.2m}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3m}$ (Age^4 x Distance^2)	-	-	-	-
$\beta_{5.1m}$ (Age^5)	-7.91E-09	.005	-7.57E-09	.012
$\beta_{5.2m}$ (Age^5 x Distance)	1.00E-09	.024	-	-
$\beta_{5.3m}$ (Age^5 x Distance^2)	-	-	-2.01E-11	.101

Table 3.16. Backward linear regression for the effect of a household member on anthropometrics and CariesR as a function of age, sex, and distance to the main road, with wealth controls

	BMIR		CariesR	
Parameter	**β**	**p**	**β**	**p**
Intercept	-1.06E-01	.787	3.73	.002
Dist	-	-	-1.11	.001
Distance^2	-	-	4.92E-02	.009
Cattle	-	-	-3.17E-01	.144
Pasture	-2.09E-02	.014	-2.25E-02	.072
Timber	-3.07E-02	.037	-	-
Cash Crops	2.12E-01	.122	2.51E-01	.209
Females				
$B_{0.1f}$ (n_f)	7.47E-01	.005	-9.72E-01	.001
$B_{0.12f}$ (n_f x Distance)	-9.41E-02	.002	2.22E-01	.000
$B_{0.3f}$ (n_f x Distance^2)	-	-	-7.60E-03	.001
$\beta_{1.1f}$ (Age)	-6.14E-02	.009	-	-
$\beta_{1.2f}$ (Age x Distance)	5.80E-03	.018	-	-
$\beta_{1.3f}$ (Age x Distance^2)	-	-	-	-
$\beta_{2.1f}$ (Age^2)	-	-	-	-
$\beta_{2.2f}$ (Age^2 x Distance)	-	-	-	-
$\beta_{2.3f}$ (Age^2 x Distance^2)	-	-	-	-
$\beta_{3.1f}$ (Age^3)	-	-	2.77E-05	.064
$\beta_{3.2f}$ (Age^3 x Distance)	-	-	-1.63E-05	.002
$\beta_{3.3f}$ (Age^3 x Distance^2)	-	-	-	-
$\beta_{4.1f}$ (Age^4)	-	-	-	-
$\beta_{4.2f}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3f}$ (Age^4 x Distance^2)	-	-	9.55E-09	.023
$\beta_{5.1f}$ (Age^5)	1.93E-08	.003	-	-
$\beta_{5.2f}$ (Age^5 x Distance)	-1.76E-09	.007	3.85E-09	.006
$\beta_{5.3f}$ (Age^5 x Distance^2)	-	-	-	-
Males				
$B_{0.1m}$ (n_m)	-5.71E-01	.005	-	-
$B_{0.12m}$ (n_m x Distance)	1.34E-01	.018	1.33E-01	.006
$B_{0.13m}$ (n_m x Distance^2)	-6.68E-03	.007	-6.84E-03	.016
$\beta_{1.1m}$ (Age)	-	-	-2.93E-02	.028
$\beta_{1.2m}$ (Age x Distance)	-7.83E-03	.013	-	-
$\beta_{1.3m}$ (Age x Distance^2)	5.59E-04	.001	-	-
$\beta_{2.1m}$ (Age^2)	1.75E-03	.002	-	-
$\beta_{2.2m}$ (Age^2 x Distance)	-	-	-	-
$\beta_{2.3m}$ (Age^2 x Distance^2)	-	-	8.58E-06	.022
$\beta_{3.1m}$ (Age^3)	-	-	2.51E-05	.064
$\beta_{3.2m}$ (Age^3 x Distance)	-2.26E-06	.114	-	-
$\beta_{3.3m}$ (Age^3 x Distance^2)	-	-	-	-
$\beta_{4.1m}$ (Age^4)	-	-	-	-
$\beta_{4.2m}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3m}$ (Age^4 x Distance^2)	-	-	-	-
$\beta_{5.1m}$ (Age^5)	-6.35E-09	.002	-6.16E-09	.033
$\beta_{5.2m}$ (Age^5 x Distance)	6.25E-10	.066	1.14E-09	.158
$\beta_{5.3m}$ (Age^5 x Distance^2)	-	-	-1.54E-10	.038

Table 3.16. (continued)

	BMIR		CariesR	
Parameter	**β**	**p**	**β**	**p**
Intercept	-1.06E-01	.787	3.73	.002
Dist	-	-	-1.11	.001
Distance^2	-	-	4.92E-02	.009
Cattle	-	-	-3.17E-01	.144
Pasture	-2.09E-02	.014	-2.25E-02	.072
Timber	-3.07E-02	.037	-	-
Cash Crops	2.12E-01	.122	2.51E-01	.209
Females				
$B_{0.1f}$ (n_f)	7.47E-01	.005	-9.72E-01	.001
$B_{0.12f}$ (n_f x Distance)	-9.41E-02	.002	2.22E-01	.000
$B_{0.3f}$ (n_f x Distance^2)	-	-	-7.60E-03	.001
$\beta_{1.1f}$ (Age)	-6.14E-02	.009	-	-
$\beta_{1.2f}$ (Age x Distance)	5.80E-03	.018	-	-
$\beta_{1.3f}$ (Age x Distance^2)	-	-	-	-
$\beta_{2.1f}$ (Age^2)	-	-	-	-
$\beta_{2.2f}$ (Age^2 x Distance)	-	-	-	-
$\beta_{2.3f}$ (Age^2 x Distance^2)	-	-	-	-
$\beta_{3.1f}$ (Age^3)	-	-	2.77E-05	.064
$\beta_{3.2f}$ (Age^3 x Distance)	-	-	-1.63E-05	.002
$\beta_{3.3f}$ (Age^3 x Distance^2)	-	-	-	-
$\beta_{4.1f}$ (Age^4)	-	-	-	-
$\beta_{4.2f}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3f}$ (Age^4 x Distance^2)	-	-	9.55E-09	.023
$\beta_{5.1f}$ (Age^5)	1.93E-08	.003	-	-
$\beta_{5.2f}$ (Age^5 x Distance)	-1.76E-09	.007	3.85E-09	.006
$\beta_{5.3f}$ (Age^5 x Distance^2)	-	-	-	-
Males				
$B_{0.1m}$ (n_m)	-5.71E-01	.005	-	-
$B_{0.12m}$ (n_m x Distance)	1.34E-01	.018	1.33E-01	.006
$B_{0.13m}$ (n_m x Distance^2)	-6.68E-03	.007	-6.84E-03	.016
$\beta_{1.1m}$ (Age)	-	-	-2.93E-02	.028
$\beta_{1.2m}$ (Age x Distance)	-7.83E-03	.013	-	-
$\beta_{1.3m}$ (Age x Distance^2)	5.59E-04	.001	-	-
$\beta_{2.1m}$ (Age^2)	1.75E-03	.002	-	-
$\beta_{2.2m}$ (Age^2 x Distance)	-	-	-	-
$\beta_{2.3m}$ (Age^2 x Distance^2)	-	-	8.58E-06	.022
$\beta_{3.1m}$ (Age^3)	-	-	2.51E-05	.064
$\beta_{3.2m}$ (Age^3 x Distance)	-2.26E-06	.114	-	-
$\beta_{3.3m}$ (Age^3 x Distance^2)	-	-	-	-
$\beta_{4.1m}$ (Age^4)	-	-	-	-
$\beta_{4.2m}$ (Age^4 x Distance)	-	-	-	-
$\beta_{4.3m}$ (Age^4 x Distance^2)	-	-	-	-
$\beta_{5.1m}$ (Age^5)	-6.35E-09	.002	-6.16E-09	.033
$\beta_{5.2m}$ (Age^5 x Distance)	6.25E-10	.066	1.14E-09	.158
$\beta_{5.3m}$ (Age^5 x Distance^2)	-	-	-1.54E-10	.038

DISCUSSION

The goal of this study was to use a pooled resource model to assess the differential effects of Shuar family members on growth across ecological circumstances and to test several predictions derived from life history theory. We first predicted that juveniles would have negative effects on one another's growth, indicating competition for resources and a quantity-quality trade-off for parents. We find strong support for this prediction. Using a consumer-to-producer ratio with producers defined as females over age fifteen, additional consumers caused significant reductions in height. Moreover, consumers interacted with producers as predicted, with additional producers offsetting the effect of additional consumers. When we moved to the pooled resource model to control for the effects of all family members we found a generally consistent pattern in which juveniles had detrimental effects on the height (Figure 3.10), weight (Figure 3.11), and caries (Figure 3.13) of other juveniles. Effects on BMI (Figure 3.12) were somewhat more complicated, most likely due to unequal effects on height and weight.

Before discussing the other results, we should first address the question of the appropriateness of each growth measure as a measure of "quality". When we talk about quality in an evolutionary sense, the only qualities that matter are those that eventually affect either survival, reproduction, or the success of successive generations. More generally, to be a measure of quality, the characteristic in question must affect fitness. Some studies have attempted to address fitness more directly, by assessing effects on mortality, lifetime reproduction, or grand-offspring production (e.g., Blurton Jones & Nicholas, 1986; Borgerhoff Mulder, 2000; Gillespie *et al.*, 2008; Hill & Hurtado, 1996;

Sear *et al.*, 2002). Other studies have used "fitness proxies", that is, indicators that are expected to be related to fitness at some point down the road, such as anthropometric measures (e.g., Hagen & Barrett, 2009; Hagen *et al.*, 2006) or academic performance (Angrist *et al.,* 2006; Hanushek, 1992; Kaplan *et al.*, 1995; Patrinos & Psacharopoulos, 1997). As Hagen *et al.* (2006) have pointed out, measuring mortality may miss the smaller effects of trade-offs that might have been important in ancestral populations, or trade-offs that only have an effect on mortality during times of stress.

In this paper we evaluate three anthropometric measures as potential fitness proxies: height-for-age, weight-for-age, and BMI-for-age. In terms of fitness, what do each of these measures represent? Deficits in height and weight are related not only to mortality risk (Pelletier & Frongillo, 2003; Victora, 1992) but to multigenerational effects. Maternal height is related to child survival and growth (Subramanian *et al.*, 2009) and to risk of obstetrical complication (Prasad & Al-Taher, 2002). Thus, the effects of reduced height might have fitness implications that are only apparent after multiple generations. Additionally, increased body size is associated with increased social status and dominance (Von Rueden *et al.*, 2008), and increased mate value and short term matings, especially for males (Buunk *et al.,* 2007; Pawlowski & Koziel, 2002; Rhodes *et al.*, 2005).

Thus, it is reasonable to think of these as fitness proxies. However, there are also good reasons to consider anthropometrics independent of their value as proxies. As a number of authors have pointed out (e.g., Hill & Hurtado, 1996), parents are unlikely to make the mistake of having so many children that it reduces lifetime completed fertility.

Such drastic mistakes would likely have strong selection against them or to be met by strategies such as infanticide. However, parents might readily surpass the optimum by a small margin, enough to reduce qualities such as height which are beneficial, but perhaps not always necessary for success. Moreover, there might be multiple optimal solutions to the quantity-quality problem that reflect energetic trade-offs but do not affect fitness. To use a crude example, the average fitness from five small children might be equivalent to the average fitness from four large children. There is still a trade-off, but the trade-off will not be reflected in net fitness. However, despite having the same average fitness, there might be strategic reasons for some parents to exchange height for increased reproduction while others do better with fewer large offspring. For example, if wealth or status is inherited the offspring of high status individuals may have less need to compete for mates or resources, and therefore less need for large body size. Higher status individuals might therefore be better served by producing more, smaller offspring.

In this study we found similar, but not identical results for our three anthropometric measures. What are the implications of each? A commonly repeated maxim is that stunting (low height-for-age) represents chronic shortages, whereas deficits in weight, such as wasting (low weight-for-age), represent acute shortages, with low weight preceding low height (Fernandez *et al.,* 2002; Walker *et al.*, 1996). However, this may not be accurate for indigenous South American populations. In South America, stunting is common but wasting is almost nonexistent (Victora, 1992), a pattern that holds for the Shuar who have high levels of stunting but very low levels of wasting (Blackwell *et al.*, 2009). Moreover, in South America, rates of stunting are correlated

with child mortality rates, whereas wasting is not (Victora, 1992). This is likely not because wasting is unrelated to mortality, but because wasting is uncommon enough in South America for the effect to appear insignificant. In South America, height seems to be much more affected by individual conditions than weight. In this study, for example, household accounted for about 8% of the variation in height, but only 1% of the variation in weight. Height also has a greater correlation with immune function biomarkers related to pathogen exposure than does weight (Chapter V). Thus, there are a number of reasons why height may be the most sensitive measure of trade-offs, at least for Amazonian populations.

Growth in height represents an investment into additional skeletal, muscular, and other components that necessitate continued energy investment over the lifespan. Although survival may be impacted by height through ability to do physical work, part of the benefit of height for males is likely to be increased status or attractiveness, and thus increased mating opportunities. Thus, height growth above the amount needed to do work can be considered investment into future mating effort. In contrast, weight growth may be in the form of muscle or fat. Muscular growth may be similar to height growth or may increase resource extraction abilities. In contrast, increases in adiposity impose far lower maintenance costs, and instead should be thought of as stored energy, rather than spent energy. In examining the results of the pooled resource model, then, we should pay careful attention to who is affecting height, who weight, and where these overlap (Figure 3.14). Where there is a positive effect on BMI, we should note where it is associated

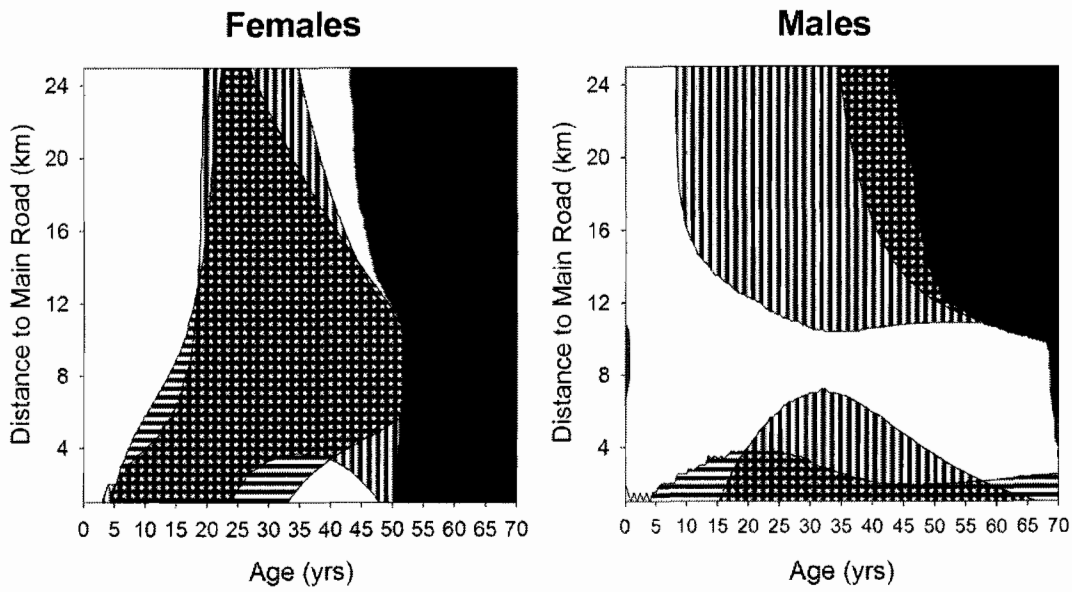

Figure 3.14. Overlap in effects on height (positive effects, horizontal stripes) and weight (vertical stripes) for males and females, based on the pooled resource model. Negative effects on both are in white and areas not represented by samples are masked in black.

with decreased height, representing shifting energy away from height and into weight, and where it is associated with increased height, representing investment into both dimensions of growth.

The second hypothesis to be tested in this study was that caregivers would have significant effects on the children in their households, but that the exact nature of the contributions would vary according to ecological constraints. Specifically, we predicted that the effect of reproductive age females would be relatively constant across contexts, but that the effects of adolescents and males would vary with context. The actual results proved to be a bit more complicated. Females age approximately 20-30 have positive effects on both height and weight, regardless of geography (Figure 3.14). And,

throughout most of the villages, reproductive age females continue to have strong positive effects. However, we were surprised to find that females age 30-50 or so have negative effects on growth in both the nearest villages and the most distant. Interestingly, these are also the areas where males have positive effects on both height and weight, and the areas where height and weight are the greatest. In the villages closer to the main road, adolescent females also appear to make up for some of the negative effect of older females. It may be that in these areas females have negative effects because they are able to spend more time in lactation due to investment from alternative sources. The additional energy needed for lactation might cause them to compete for resources. However, this interpretation is highly speculative and we do not presently have any direct data to support it.

The effects of adolescents also vary with context. In the nearest villages both male and female adolescents, and perhaps older juveniles, have positive effects on height. Male adolescents also have positive effects in more distant villages, although only on weight (and consequently BMI). In contrast, adolescent females do not have positive effects in these villages. This is consistent with the findings of Hagen and Barrett (2009). They studied a Shuar village located in Pastaza (to the north of the Upano Valley area considered in this study) and found that adolescent brothers had positive effects on BMI while adolescent sisters had negative effects.

The effects of older males also vary, although perhaps less than expected. In towns close to the main road, adult males have positive effects on both height and weight, consistent with predictions about the involvement of males in market economies. In

intermediate villages males have strong negative effects that increase with age. In the most distant villages, younger adult males have positive effects on weight but not height. Only at older ages do males have positive effects on both height and weight (Figure 3.14). The effect of males age 15-40 on weight but not height in distant villages is difficult to interpret. Are these males causing juveniles to shift energy away from height gain into weight gain? If so, then perhaps they are providing resources, but inconsistently. Another possibility is that the timing of investment is critical, or that specific nutrients (such as protein) are involved. Finally, hygiene and access to medical care might have significant effects on pathogen exposure and recovery, which affects relative investment into height and weight.

Clearly, more work is needed to parse out the details of why certain household members have the effects they do in certain circumstances. What our results do show is the utility of a pooled resource model for parsing out the effects of different individuals on juvenile growth and family wealth variables. Although the model is essentially a curve fitting procedure that is more descriptive in nature than appropriate for hypothesis testing, it provides an accurate description of the effects of particular kin in the villages studied and yields continuous age and sex functions that likely reflect reality more closely than discrete categorical analyses. As such, it provides a strong foundation for future analyses to examine the mechanisms through which these kin effects occur.

BRIDGE TO CHAPTER IV

Chapter II examined the growth of Shuar children in relation to other groups, while in this chapter I examined growth as it varies between Shuar families and villages. In Chapter IV I turn to the examination of immune function the patterns that emerge from the dynamics of pathogen transmission. Chapter IV examines the age patterning of immunoglobulin E (IgE) in three populations: the Shuar, the Tsimane of Bolivia, and the United States. These three populations experience different degrees of market integration and different degrees of exposure to helminths, which are a primary cause of elevated IgE levels. Chapter IV expands our consideration of life history trade-offs by examining how early events direct the development of immune responses. Chapter IV also serves as an introduction to IgE and a bridge to Chapter V, in which I return to the examination of growth and the effects of family members as they relate to IgE and CRP, another biomarker of investment into immune function.

CHAPTER IV

EVIDENCE FOR A PEAK SHIFT IN HUMORAL RESPONSES TO HELMINTHS: AGE PROFILES OF IMMUNOGLOBULIN E (IGE) IN THE SHUAR OF ECUADOR, THE TSIMANE OF BOLIVIA, AND THE U.S. NHANES

This chapter is co-authored with J. Josh Snodgrass, Michael Gurven, Hillard Kaplan, Felicia C. Madimenos, and Lawrence S. Sugiyama. Snodgrass, Madimenos, and Sugiyama were all central members of the team that collected the Ecuadorian data. Gurven and Kaplan collected the Tsimane data which is used as a comparative sample. Josh Snodgrass made his lab available for analyses and provided critical expertise in the analysis of dried blood spots. Lawrence Sugiyama is director of the Shuar Life History project and as such directed the fieldwork upon which this chapter is based. The author of this dissertation proposed the work contained, obtained funding, and collected samples in Ecuador. The analyses, writing, and figures contained in this chapter are the work of the author of this dissertation.

INTRODUCTION

Intestinal helminths such as roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*), hookworm (*Necator americanus*, *Ancylostoma duodenale*, *A. ceylanicum*, *A. braziliense*) and threadworm (*Strongyloides stercoralis*) infect around a billion people worldwide. Helminths can cause anemia and may increase susceptibility to other diseases (Dreyfuss et al., 2000; Bundy et al., 2000; Borkow et al., 2000).

However, because they are subtle, the health effects of helminths are often overlooked or underappreciated (Hotez *et al.,* 2008; Hurtado *et al.*, 2004; Hurtado *et al.*, 2008). Perhaps as a consequence, we have only begun to understand the mechanisms of immune response to helminths, the ways in which helminths manipulate host immunity (Hewitson *et al.,* 2009; Maizels & Yazdanbakhsh, 2003; Maizels, 2005), and the dynamics of helminth transmission (Galvani, 2005; Woolhouse & Hagan, 1999; Woolhouse, 1998).

One of the ways the immune system defends against parasites is by producing antibodies (known as immunoglobulins) which circulate in the blood and bind to antigens on the surface of pathogens. Immunoglobulins (Ig) come in several distinct classes, including IgG, IgA, IgE, and IgM. The relative balance of immunoglobulin types is determined in part by the balance of T cell subtypes in the host immune system. The major T cell subtypes are known as T_H1 and T_H2.

Helminth infections are associated with a general shift in the host immune system towards a T_H2 biased phenotype, characterized in particular by increased production of immunoglobulin E (IgE) (Maizels & Yazdanbakhsh, 2003; Maizels, 2005). However, it is unclear whether IgE is protective of the host or whether the increase in IgE may in part be due to parasite manipulation of host immunity. Among populations with endemic helminth infection, individuals with higher levels of IgE often show increased resistance to reinfection and lower parasite loads (Faulkner *et al.,* 2002; Hagan *et al.*, 1991; Hagel *et al.*, 2006; McSharry *et al.*, 1999). However, other studies have found that IgE rises with infection and falls with antihelminth treatment (Cooper *et al.,* 2008; Hagel *et al.*, 1993). Thus, some have hypothesized that helminths promote IgE synthesis in order to saturate

host mast cells and block an effective response or to promote the excretion of eggs from the host system, facilitating parasite transmission (Maizels & Yazdanbakhsh, 2003).

Although the issue of whether IgE plays a protective role against helminth infection is contested, what is clear is that populations with significant helminth burdens also have significantly elevated levels of IgE compared to North Americans and Europeans. In Western populations, high IgE is usually associated with allergic diseases such as asthma, diseases that are often very rare in populations with significant helminth burdens. Thus, it has been hypothesized that helminth infections protect against allergy, either by monopolizing T_H2 responses leaving few immune system resources for allergic responses (Yazdanbakhsh *et al.*, 2002), or by affecting the development of the immune system during childhood and even *in utero* so that T_H2 cells respond appropriately to pathogens instead of reacting inappropriately to allergens (Ege *et al.,* 2006; Holt & Jones, 2000; King *et al.*, 1998; Riedler *et al.*, 2001).

Despite the probable importance of early events in the "tuning" of immunologic responses, no studies have carefully examined the early age patterning of IgE expression in populations with high helminth endemicity. However, there are reasons to predict significant age patterning. Helminth infections show characteristic age patterning, peaking around puberty and then declining during adulthood (Faulkner *et al.,* 2002; Hurtado *et al.*, 2008; Wahyuni *et al.*, 2005). The exact timing of the peak in helminth infections, however, may depend upon parasite transmission rates and prevalence, with infections tending to peak earlier to populations with higher transmission (Anderson & May, 1985; Woolhouse, 1998) or lower strain diversity (Galvani, 2005). This "peak

shift" results from the interaction between the rate at which new individuals are infected and the rate at which immunity is acquired. When transmission is higher, infection occurs more quickly, but immunity is also acquired more quickly. Once a sufficient number of individuals gain immunity, prevalence declines. Peak shifts have been shown for helminth (Woolhouse, 1998), and for certain humoral responses to *Schistosoma haematobium* (Mutapi *et al.*, 1997). If IgE is responding to helminth infections, we might expect a corresponding peak shift in IgE levels. Although a number of studies have reported that IgE increases quickly in the first five to ten years of life and then levels off (Grundbacher, 1975; Johnson *et al.*, 1998; Lindberg & Arroyave, 1986; Petridou *et al.*, 1995), these studies have all used broad five or ten year age categories, making identification of peaks in IgE difficult.

In addition to understanding the peak shift, knowledge of the age patterning of IgE provides a baseline for understanding the effect of early immunological events on immunological phenotypes, and how those effects are perpetuated throughout the lifespan. For example, one study found that adolescent Ethiopians infected with helminths who immigrated to Israel and were subsequently treated continued to have high IgE levels one year later despite a lack of reinfection (Iancovici Kidon *et al.*, 2005). However, Ethiopian adolescents who had migrated to Israel seven years or more before, when they were on average seven years old, had significantly lower IgE levels when measured, suggesting that the timing of helminth removal was critical to future IgE.

Finally, part of the difficulty many studies have had in determining whether IgE serves a protective role may be due to an insufficient accounting for the effects of age.

Simply controlling for age as a linear variable may be insufficient, both because the age/IgE relationship may be non-linear and because IgE levels may indicate different things at different ages. Early immune responses to helminths are likely polyclonal. Only after clonal selection has occurred does the IgE repertoire become dominated by useful antibodies. The age at which this occurs may vary between populations depending on the rate of transmission as well as the rate of helminth maturation within infected individuals (Woolhouse & Hagan, 1999).

To address part of this need, the current study describes in detail the age and sex patterning of IgE levels in three populations expected to have different levels of macroparasite exposure. In particular, we examine whether there is a peak shift in humoral response to helminths, just as there appears to be in helminth infections.

METHODS

Study Populations

Shuar. Shuar are Amerindians from the Amazonas region of Ecuador, closely related to other groups such as the Achuar and Shiwiar who belong to what has been known as the Jivaroan language group (Descola, 1994; Descola, 1996; Harner, 1984). Traditionally, Shuar lived in scattered clusters of a few households, their economy based on horticulture, hunting, and fishing. Our previous work has shown that approximately 40% of Shuar children are stunted, and that Shuar are much more likely to be stunted than both the closely related Shiwiar and Achuar, as well as non-indigenous children living in the

same area (Blackwell *et al.*, 2009). Although we know of no studies examining helminth infections in the Shuar, per se, recent studies report infection rates of around 50% in other Amazonian Ecuadorian populations, with *Ascaris* the most prevalent parasite. These include children in rainforests villages on the western side of the Andes (Sackey *et al.*, 2003) and Napo Runa children from the Rio Napo area in northwestern Amazonas (San Sebastian & Santi, 1999; San Sebastian & Santi, 2000).

The data for this study was collected by ADB, JJS, FCM, and LSS as part of the Shuar Life History Project (www.uoregon.edu/~sugiyama/shuar) in a village of approximately 500 people, located approximately 45 minutes by truck from the town of Sucúa, Ecuador. The dirt road to the village has only been improved in the last few years, before that the village was reached only on foot. No one in the village owns a car, but a truck comes through about once a day to offer travel to Sucúa (providing service much like a bus). Many adults travel to Sucúa once every week or two. Since 2000, the village has had a health clinic staffed by an auxillary or nurse that provides vaccinations and dispenses basic medications such as albendazol for parasites, and antiboiotics, acetaminophen, and vitamins for most everything else. The village also has a primary school, which most children attend. There is a water line that pipes untreated water from a spring through the central part of the village, and houses along this central road have spigots. Other houses obtain water either from their neighbors or from nearby streams. We collected household inventories which show that about 80% of households get their water from the water line. About 70% of households have outhouses (almost all without water), the rest typically use the forest and other open spaces. Electricity arrived in 2000

and 45% have electricity which can be used for multiple purposes, while 20% have electricity only for light, and 30% have no electricity.

All participants gave informed consent or assent, with both parental consent and child assent for subjects under fifteen. The study was approved by the village leaders, the Ministerio de Salud Pública de Morona Santiago, the Federacíon Interprovincial de Centros Shuar (FICSH), and the Institutional Review Board of the University of Oregon.

Tsimane. Tsimane are lowland forager-horticulturalists that live along the Maniqui River in Bolivia. Tsimane subsist primarily on cultivation of rice, corn, manioc, and plantains, as well as hunting fishing, and gathering. Like the Shuar, Tsimane are undergoing rapid acculturation, and subsistence varies across villages, with corresponding changes in subsistence and social organization (Brabec *et al.,* 2007; Vadez *et al.*, 2004). Tsimane show high levels of inflammatory markers, such as C-reactive protein (Gurven *et al.,* 2008; Gurven *et al.*, 2009; McDade *et al.*, 2005). Helminth infections are highly prevalent, with hookworm being the predominant parasite, infecting about 76% of children age two to eleven (Tanner *et al.*, 2009). Like the Shuar, stunting is quite prevalent among the Tsimane, with about 40-50% of Tsimane classified as stunted (Benefice *et al.,* 2006; Foster *et al.*, 2005). The data for this study was collected in sixteen villages representing the range of Tsimane circumstances. Data was collected as part of the Tsimane Life History Project by MG, HK and colleagues (http://www.unm.edu/~tsimane/). Informed consent was obtained for all participants, and the study was approved by the Institutional Review Boards at the University of New

Mexico, University of California-Santa Barbara, as well as the *Gran Consejo* Tsimane and community officials for the communities involved.

National Health and Nutrition Examination Survey (NHANES). NHANES is a large scale, national survey of health, nutrition, and social factors conducted by the National Center for Health Statistics and Center for Disease Control. This study uses data from the NHANES 2005-2006 dataset (http://www.cdc.gov/nchs/nhanes/nhanes2005-2006/nhanes05_06.htm). The data was collected under a complex stratified sampling scheme that increases the representation of minorities and normalizes age distribution, and so is not strictly a random cross-section of the United States. NHANES data does include a weighting variable that can be used to weight individuals in the study according to the percent of the U.S. population with which they share demographic and geographic characteristics; however, for the purposes of this study we did not use these sample weights. Thus, the NHANES results presented here are accurate for the NHANES sample, but strictly speaking does not reflect the composition of the U.S. population as a whole. The sample presented here includes 8,336 individuals. The ethnic breakdown of the sample is as follows: 27% Mexican-American, 36% Caucasian, and 26% African-American, with the remainder composed of other ethnic identities. Eighty-eight percent are U.S. citizens. Fifty-two percent of the sample is female.

Blood Collection and Analysis

Shuar. Shuar samples were collected following standard procedures to collect dried blood spots (McDade *et al.*, 2007). A finger prick using a sterile, disposable lancet was used to obtain three to five 50μL drops of whole capillary blood spotted onto standardized filter paper (No. 903; Whatman [formerly Schleicher & Schuell]). Blood spot samples were dried for four hours and then sealed in airtight bags and frozen in the village clinic freezer for one to three weeks. Blood spots were kept cold with freezer packs for transport to the Ecuadorian capital, Quito. They were allowed to come to room temperature for transport by plane to the University of Oregon (approximately 12 hours), after which they were stored at -30ºC until analysis.

IgE levels were determined by ELISA following a commercially available protocol (Bethyl Labs, Inc.: #E80-108 and #E101) adapted for use with blood spots (Tanner & McDade, 2007). Briefly, calibrators were made by serially diluting Human IgE calibrator (Bethyl; #RC80-108) and then mixing each dilution with the same volume washed erythrocytes (McDade *et al.*, 2004) to produce seven calibrators ranging from 9,000 to 140.6 ng/ml (3,750 IU/ml to 58.6 IU/ml), as well as a zero standard. Commercially available sera with known IgE levels (Bio-Rad; Liquichek Immunology Control; #590X) was also diluted 1:2 with erythrocytes. 50 μl drops of calibrators and controls were spotted onto filter paper and frozen.

The evening before the assay one 3.2 mm circle was punched from each blood spot card sample, calibrator, and control, and eluted in 250 μl sample diluent made by mixing 100ml post-coat solution (50 mM Tris buffered saline, 1% BSA; pH 8.0, Sigma

Chemical #T6789) with 0.5 ml 10%Tween 20. Coating antibody (Bethyl #A80-108A) was diluted 1:100 in coating buffer (0.05 M carbonate-bicarbonate, pH 9.6, Sigma Chemical #C3041) and 100µl was added to each well in a ninety-six well plate (Nunc MaxiSorp #445101). Plates and diluted samples were incubated overnight at 4°C. In the morning, wells were aspirated and washed with wash solution (50 mM Tris buffered saline, pH 8.0, 0.05% Tween 20; Sigma Chemical # T9039) in an automated plate washer. Wells were then blocked for 30 minutes in blocking solution (50 mM Tris, 0.14 M NaCl, 1% BSA, pH 8.0) and washed again. Next, each diluted sample, control, and standard was pipetted onto the plate in duplicate, 100 µl per well, and incubated for 30 minutes. Plates were again aspirated and washed, and then 100 µl 1:25,000 detection antibody (goat anti-Human IgE-HRP conjugate, 1 mg/ml; Bethyl, #A80-108P) was added to each well for 60 minutes. Plates were again washed and then incubated for 30 min at room temperature with 100 ml of chromogenic solution (TMB peroxidase substrate and peroxidase solution B; Kirkegaard & Perry). Stop solution (2 M H2SO4) was added and the plate was read at 450 nm in a ELx808 Plate reader (BioTek Instruments, Inc; Winooski, VT). Unknown concentrations and CV values were calculated automatically using a four-parameter standard curve in the Gen5 software program (BioTek Instruments, Inc; Winooski, VT).

Tsimane. Tsimane blood samples were collected by venipuncture during annual medical exams conducted by Bolivian medical doctors. Samples were centrifuged to separate serum, which was frozen in liquid nitrogen and keep frozen during transport to New

Mexico. Samples were analyzed for Total IgE (catalog: L2KIE6) by TriCore Laboratories (Albuquerque, NM) using an Immulite 2000 instrument (Siemens Corp; Deerfield, IL).

NHANES. NHANES samples were collected by venipucture during NHANES interviews by trained phlebotomists (http://www.cdc.gov/nchs/nhanes/nhanes2005-2006/nhanes05_06.htm). Determination of total IgE was done using the ImmunoCAP 1000 system (Pharmacia Diagnostics) by the Department of Pathology Immunology Laboratory at Elmhurst Memorial Hospital, Elmhurst, IL. Complete details can be found on the NHANES website at http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/al_ige_d_met_specific_ige_total_ige.pdf.

Comparability of Blood Samples. A potential limitation of this analysis is that different methods were used to determine IgE levels in these three populations. In particular, Shuar IgE levels were determined from dried blood spots, while Tsimane and NHANES levels were determined from serum. However, the use of different methods is unlikely to affect IgE determinations significantly enough to change the results of comparisons. First, the ELISA procedure used to determine blood spot IgE in this study has been evaluated for linearity and consistency and validated against controls with known IgE levels (Tanner & McDade, 2007). In this study we also ran IgE with serum-based controls that had been spotted onto filter paper. Values for controls were all within the ranges given by the manufacturer. Second, although the ELISA procedure we use here

has not been validated against matched serum samples, IgE levels in matched serum and capillary blood spots have been compared by both radioallergosorbent assay (Stapel *et al.*, 2004) and in a similar ELISA procedure (Terhell *et al.,* 2001). In both procedures serum and dried blood spot IgE levels were found to be virtually identical. The use of different methods to determine IgE levels is therefore likely to add relatively little error.

Age Estimation

Approximate birthdates were available for most Shuar children. In general, these birthdates are accurate to the month, particularly for children born after the health clinic was established in the study village in 2000. For adults, ages were less accurate, particularly for individuals older than forty. Many had birth dates on their government identification cards (by law all Ecuadorians are required to register for identification). These were used but were crosschecked with extensive genealogical information collected on individuals in the village. Geneologies included siblings and offspring, given in order of birth. Overlapping genealogies were collected from multiple informants in order to cross-check information. Tsimane age estimation was done in much the same manner. Geneologies were collected during demographic interviews done on all individuals over age 18 (n=1,098). Ages were estimated based on written records, such as those kept by Catholic missionaries in the area, photographs of people with known ages, and independent cross-checking of genealogies with multiple kin (see Gurven *et al.,* 2009). The overall sample sizes by age, sex, and population are given in Table 4.1. The Shuar data was collected with the primary goal of examining the development of immune

Table 4.1. Sample sizes by sex, population, and five year age category

	Shuar			Tsimane			NHANES		
Age	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**
0 – 5	17	13	30	5	11	16	472	466	938
6 - 10	37	34	71	23	22	45	390	384	774
11-15	14	10	24	15	11	26	560	550	1110
16-20	2	0	2	19	7	26	565	545	1110
21-25	1	1	2	25	4	29	281	203	484
26-30	3	3	6	18	15	33	279	168	447
31-35	5	0	5	8	11	19	217	181	398
36-40	4	4	8	15	15	30	188	192	380
41-45	3	2	5	14	17	31	203	187	390
46-50	2	0	2	12	7	19	178	195	373
51-55	2	1	3	11	4	15	162	165	327
56-60	1	1	2	7	7	14	145	126	271
61-65	-	2	2	7	5	12	156	176	332
66-70	-	1	1	1	1	2	140	143	283
71-75	-	-	-	1	3	4	105	129	234
76-80	-	-	-	2	4	6	85	108	193
81-85	-	-	-	2	-	2	147	145	292
Total	91	72	163	185	144	329	4273	4063	8336

function and growth in children, and so is composed of significantly more children than older adults. In contrast, the Tsimane data was collected primarily to study aging, and so contains more older-adults and relatively few young children.

Data Analysis

Prior to data analysis, all IgE values were converted into international units (1 IU = 2.4ng/ml) and natural log transformed (lnIgE), since IgE is non-normally distributed (Figure 4.1). Descriptive statistics, t-tests, and simple ANOVAs were done in PASW

Statistics 18.0 (formerly SPSS Statistics, SPSS Inc.). All other analyses were done in R 2.92 (www.r-project.org). To examine age patterning without the loss of resolution that occurs when age categories are used, we fit local regression models to the data using the R *locfit* package (Loader, 1999). Models were fit to each population sample independently. Initial models without sex were run two ways: 1) without weighting to control for uneven sex ratio in the sample, and 2) with cases weighted by a 5-year moving sex-ratio (the sex ratio for the age of the case +/- 2 years). The primary difficulty with local regression is the selection of an appropriate smoothing term. Underfitting erases important features, whereas overfitting fails to remove noise due to random variation. To remove investigator bias from the process as much as possible we fit a total of fifty-one models for each population with bandwidths ranging from 0.2-1.0 at intervals of 0.05, and local polynomial degrees ranging from one to three. A generalized cross-validation (GCV) statistic was generated for each model with the *locfit* package *gcv* command. The GCV provides a measure of model fit that is penalized for increasing degrees of freedom in the model. In general the models with relatively low GCV statistics are likely to fit the data without overfitting (Craven & Wahba, 1978). We present the models with the lowest GCV as the primary models discussed in this paper. However, since GCV alone can sometimes be misleading, we also assessed the effect of model degrees of freedom on predicted peak ages for IgE for all 153 models, and present these data as well. Ages of peak IgE were estimated for each model using the R *stats* package *optimize* function and through visual verification of the *optimize* results on

model plots. Linear models were also run in R using the *lm* function. The *anova* function was used for model comparisons.

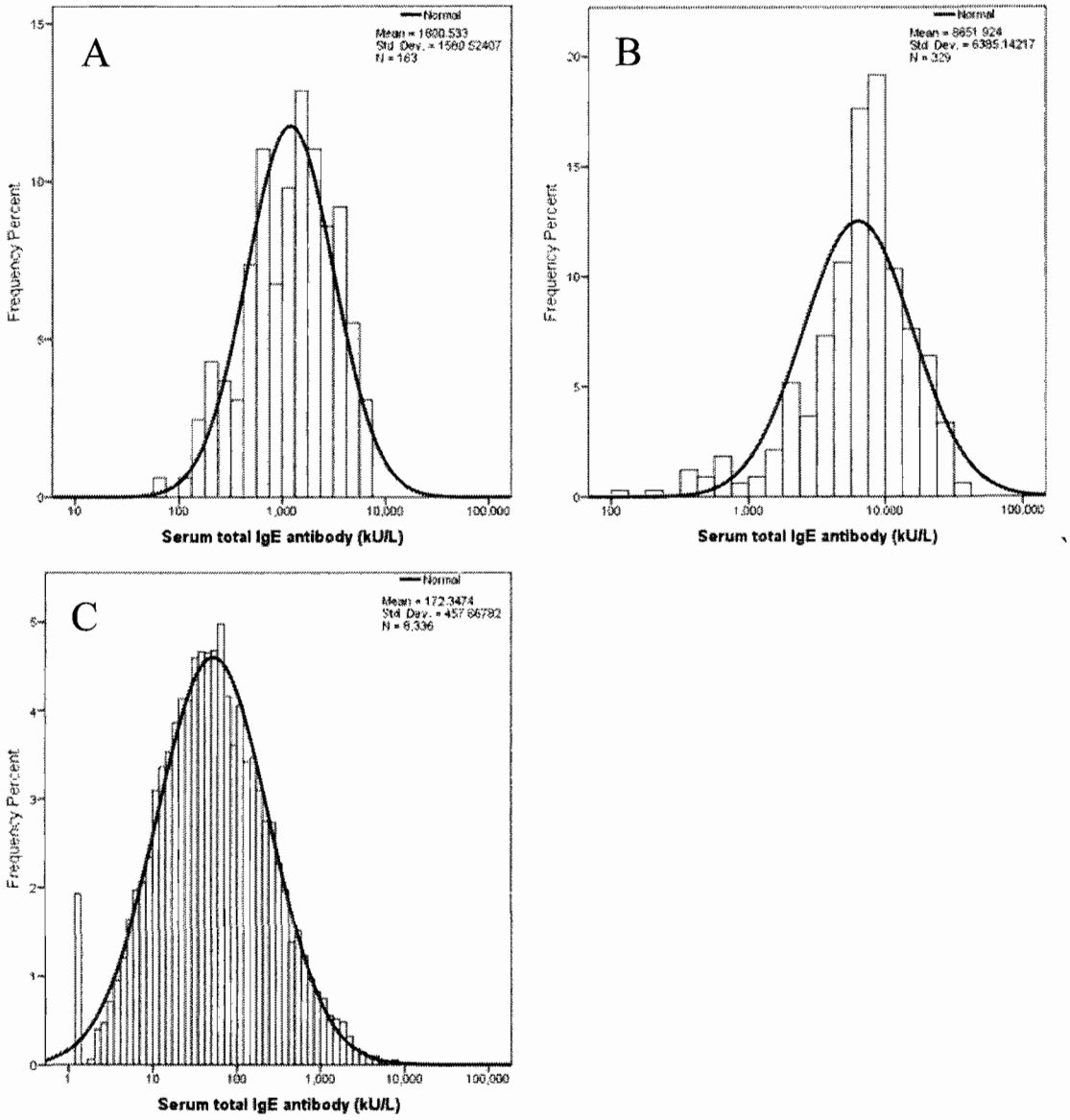

Figure 4.1. Histograms for IgE in three populations, Shuar (A), Tsimane (B), and U.S. NHANES(C). Note that x-axes are log scale both x and y axis scales differ between frames.

RESULTS

Mean IgE Values

Table 4.2 shows the mean, standard deviation, geometric mean, and log mean total IgE antibody by study population. Tsimane have the highest IgE levels (geometric mean = 6,298 IU/ml), followed by Shuar (1,196 IU/ml), and NHANES (52 IU/ml). In all three groups, males had significantly higher IgE than females (Table 4.2: all $p \leq .02$). We ran an ANOVA to test the main effects of sex and population on natural log Ige (lnIgE). The overall main effects were highly significant (Sex: $F_{1,8822} = 12.08$, $p < .01$; Population: $F_{5,8822}=1935.22$, $p < .01$) and there was no significant interaction between sex and population ($F_{2,8822}=1.47$, $p = .23$). Although the population distributions do overlap somewhat (Figure 4.2), in post-hoc pair-wise comparisons all populations were significantly different from each other (Tsimane vs. Shuar: Mean diff. = 1.66, $p < .01$; Shuar vs. NHANES: Mean diff. = 3.14, $p < .01$; Tsimane vs. NHANES: Mean diff. = 4.80, $p< .01$, all p-values use a Bonferroni correction).

Age Profile of IgE

We next examined the profile of IgE across the lifespan in these three populations. For reference mean lnIgE by five year age category is given in Table 4.3 and geometric mean IgE by age category in Table 4.4. However, since the use of age categories obscures important details such as changes within age categories and overall trends across ages, we fit local regression models to each of the three populations. GCV

Table 4.2. Mean IgE by sex and population

			Serum total IgE (IU/ml)			Natural Log IgE		
		N	Geometric Mean	Mean	SD	Mean	SD	p*
Tsimane	Females	185	5,798	7,838	5,561	8.67	.89	.06
	Males	144	7,004	9,698	7,195	8.85	.95	
	Total	329	6,298	8,652	6,385	8.75	.92	
Shuar	Females	91	1,025	1,649	1,687	6.93	1.01	.02
	Males	72	1,453	1,992	1,424	7.28	.90	
	Total	163	1,196	1,801	1,581	7.09	.98	
NHANES	Females	4273	41	127	330	3.72	1.48	<.01
	Males	4063	66	220	558	4.19	1.55	
	Total	8336	52	172	458	3.94	1.53	

*p-values indicate significance of sex difference in a 2-tailed independent samples t-test, equal variance assumed

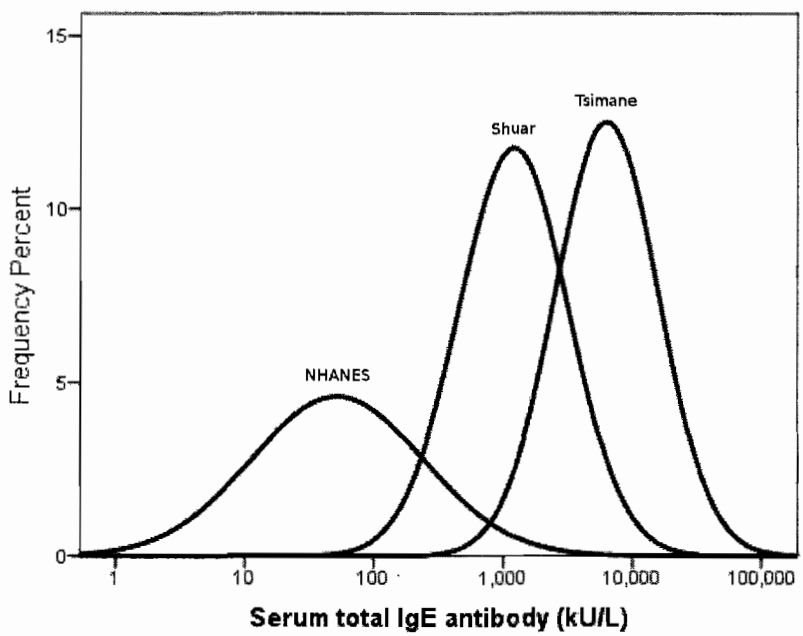

Figure 4.2. Overlay of IgE lognormal distributions for all three populations. Note that the x-axis is on a logarithmic scale.

minimization was used to select smoothing parameters, as described above. Since sex ratios are uneven for certain age ranges, particularly in the Shuar sample, we fit two models with the minimum GCV parameters, one with no weighting (Figure 4.3) and one with cases weighted according to a five year moving sex ratio (Figure 4.4). The only obvious difference between the weighted and unweighted models is in the adolescent ages for the Shuar sample. Since the Shuar sample includes no 16-20 year old males, the few females in this age category are weighted lower, resulting in some uncertainty in IgE levels for this age range. However, the ages of peak IgE predicted by the two models are almost identical. We refer to the weighted model for the remainder of this discussion.

Despite being statistically independent from one another, all three populations have similar age-related IgE profiles. In all three populations IgE increases quickly during infancy and early childhood. This is most apparent in the Shuar and NHANES samples. By age three, the youngest age in our Tsimane sample, IgE levels are nearly at the population mean. Since IgE levels in neonates are typically very low even in infected populations (Bjerke *et al.,* 1994; Croner *et al.*, 1982; Holt & Jones, 2000; King *et al.*, 1998), it is likely that most of the increase has simply occurred before the age of three, outside the range of our sample. Following the initial increase IgE plateaus, but continues to increase slowly until reaching a peak and then declining slightly to adult levels. Adult level IgE appears relatively consistent, at least within the confidence limits of the samples available. Finally in NHANES there is a small decline in IgE with old age. IgE also appears to decline in the Tsimane sample, but appears to increase in the Shuar. However, in both populations sample sizes are small in older ages.

Table 4.3. Mean natural log IgE by population

	Shuar						Tsimane						NHANES					
	Female		Male		Total		Female		Male		Total		Female		Male		Total	
Age	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
0 – 5	6.6	.9	6.9	1.3	6.7	1.1	8.6	1.1	8.6	.8	8.6	.9	3.4	1.4	3.7	1.6	3.5	1.5
6 - 10	7.3	1.0	7.4	.7	7.4	.9	9.2	.5	9.1	.8	9.1	.7	3.9	1.5	4.3	1.5	4.1	1.5
11-15	7.1	1.0	7.7	.6	7.4	.9	8.6	.9	8.6	1.4	8.6	1.1	4.0	1.5	4.3	1.5	4.2	1.5
16-20	6.0	.2			6.0	.2	8.6	.7	9.0	.6	8.7	.7	4.1	1.5	4.4	1.6	4.2	1.5
21-25	5.4		7.5		6.5	1.5	8.8	.7	9.2	.8	8.9	.7	3.7	1.5	4.4	1.6	4.0	1.5
26-30	6.5	.4	7.2	.8	6.8	.7	8.5	1.0	9.1	.8	8.8	1.0	3.7	1.5	4.3	1.6	3.9	1.5
31-35	6.9	.2			6.9	.2	8.0	1.3	8.9	.8	8.5	1.1	3.5	1.4	4.3	1.4	3.9	1.5
36-40	6.1	1.3	7.1	.6	6.6	1.1	8.6	.9	8.8	1.0	8.7	1.0	3.6	1.4	4.0	1.5	3.8	1.5
41-45	5.7	.8	6.7	.7	6.1	.9	8.9	.7	9.1	.7	9.0	.7	3.8	1.5	4.2	1.5	4.0	1.5
46-50	7.4	.4			7.4	.4	8.8	.5	8.6	1.2	8.7	.8	3.4	1.5	4.2	1.5	3.8	1.5
51-55	6.3	.4	5.4		6.0	.6	8.3	1.1	8.6	1.7	8.3	1.2	3.5	1.3	4.2	1.3	3.8	1.4
56-60	7.4		5.3		6.4	1.5	8.0	1.0	8.2	1.1	8.1	1.0	3.8	1.3	4.1	1.4	4.0	1.4
61-65			7.3	1.8	7.3	1.8	8.7	1.0	8.7	1.0	8.7	1.0	3.8	1.6	4.2	1.6	4.0	1.6
66-70			8.1		8.1		8.8		8.5		8.7	.2	3.6	1.5	4.2	1.6	3.9	1.6
71-75							9.6		9.3	.5	9.4	.4	3.4	1.5	4.0	1.5	3.7	1.5
76-80							8.8	.2	8.2	1.6	8.4	1.3	3.5	1.5	3.7	1.6	3.6	1.5
81-85							7.8	2.4			7.8	2.4	3.2	1.4	4.2	1.7	3.7	1.6
Total	6.9	1.0	7.3	.9	7.1	1.0	8.7	.9	8.9	.9	8.7	.9	3.7	1.5	4.2	1.6	3.9	1.5

Table 4.4. Geometric mean IgE by age and population

	Shuar			Tsimane			NHANES		
Age	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**
0 – 5	709	1,012	827	5,389	5,445	5,428	29	40	34
6 - 10	1,545	1,680	1,608	10,097	8,586	9,328	50	76	61
11-15	1,260	2,282	1,614	5,708	5,609	5,666	55	76	64
16-20	413		413	5,514	7,965	6,088	58	83	69
21-25	223	1,805	635	6,678	10,347	7,094	42	79	55
26-30	642	1,305	916	4,897	8,986	6,453	41	71	50
31-35	958		958	2,890	7,682	5,090	34	75	48
36-40	466	1,260	766	5,501	6,361	5,915	37	56	46
41-45	291	811	439	7,086	9,307	8,228	45	69	55
46-50	1,713		1,713	6,470	5,461	6,078	29	67	45
51-55	546	225	407	3,864	5,379	4,220	32	64	45
56-60	1,630	201	573	2,972	3,643	3,290	47	63	54
61-65		1,555	1,555	5,975	5,944	5,962	46	65	55
66-70		3,275	3,275	6,574	5,037	5,754	38	70	51
71-75				14,963	11,262	12,091	30	54	41
76-80				6,524	3,501	4,308	33	41	37
81-85				2,322		2,322	25	68	41
Total	1,025	1,453	1,196	5,798	7,004	6,298	41	66	52

To better examine the rate of change in IgE with age for the first thirty years of life, we used the *locfit* function to calculate the first derivate of the sex-weighted local regression function (Figure 4.5). The derivative graphs illustrate the points noted above, but make even more obvious the similarities between the age profiles of the Shuar and NHANES samples. The rate of change is highest after birth, but declines rapidly with age. In both populations the rate approaches zero and may even cross into negative territory before increasing again for a few years. After reaching a peak, there is a period where the slope is negative, after which the rate hovers around zero.

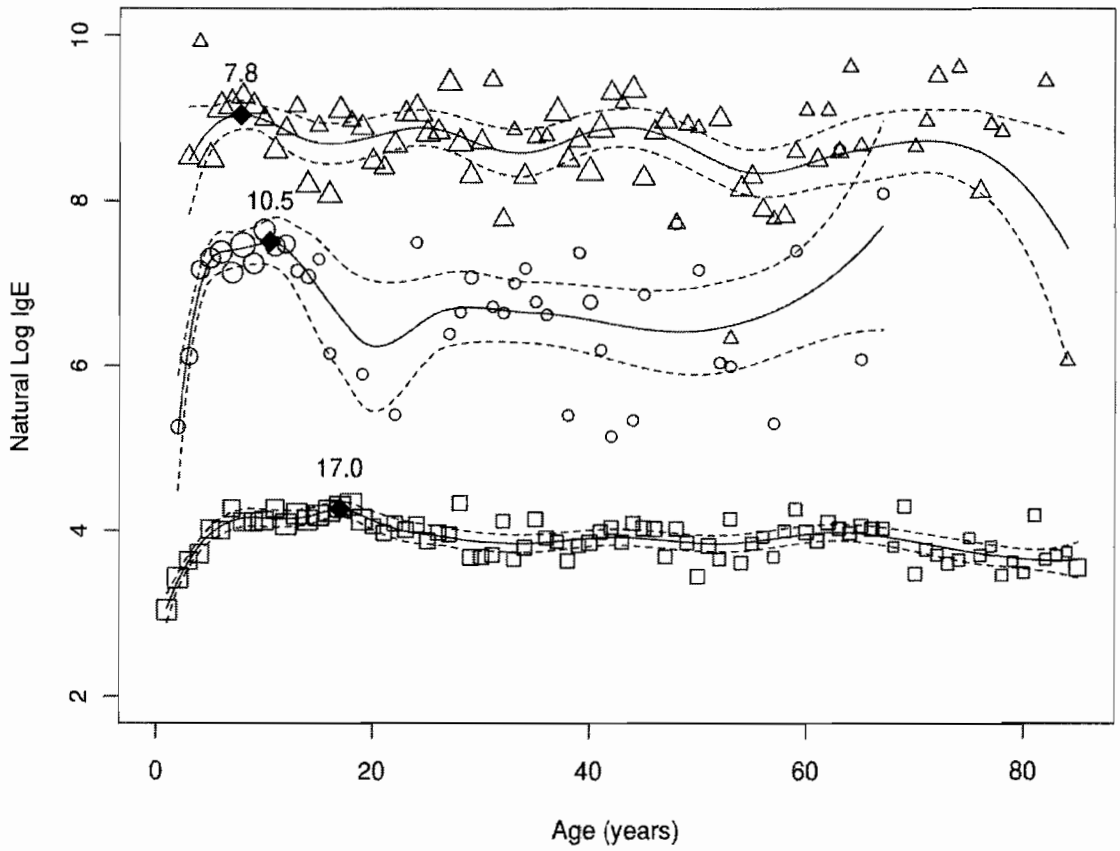

Figure 4.3. IgE by age in Tsimane (triangles), Shuar (circles), and NHANES (squares), with unweighted local regression fit lines. Points show the mean value by one year age category with the area of the point proportional to the sample size at that point. Note that NHANES points are scaled 1:20 relative to Shuar and Tsimane due to the larger NHANES sample. Dotted lines are the local 95% confidence interval for the fit. Smoothing parameters determined by GCV minimization: NHANES: alpha = 0.3, degrees=3, model df= 12.1; Shuar: alpha = 0.7, degrees=3, model df =8.0; Tsimane: alpha =0.45, degrees=3, model df=8.6.

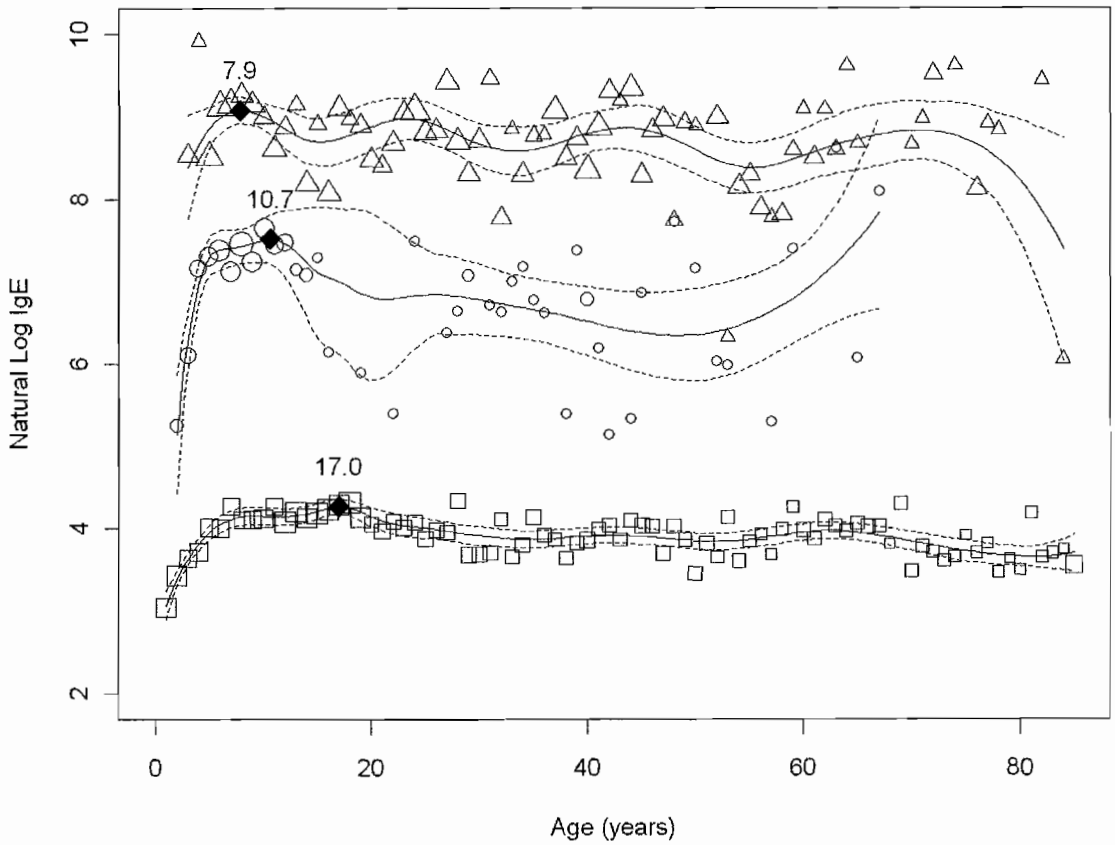

Figure 4.4. IgE by age in Tsimane (triangles), Shuar (circles), and NHANES (squares), with weighted local regression fit lines. Cases are weighted based on a moving sex ratio for the case +/- 2 year categories (five years total). Points show the mean value by one year age category with the area of the point proportional to the sample size at that point. Note that NHANES points are scaled 1:20 relative to Shuar and Tsimane due to the larger NHANES sample. Dotted lines are the local 95% confidence interval for the fit. Smoothing parameters determined by GCV minimization: NHANES: alpha = 0.3, degrees=3, model df= 12.1; Shuar: alpha = 0.7, degrees=3, model df =8.0; Tsimane: alpha =0.45, degrees=3, model df=8.6.

Both Shuar and NHANES follow this shape very closely. The key differences between the two include the overall rate of change, which is much higher in Shuar, and the timing of the rate changes. In Shuar the entire shape is essentially compressed and shifted toward earlier ages. The initial point at which the slope levels off occurs around age nine in the NHANES and around age six in Shuar. The final peak occurs around age 10 in Shuar, but around age seventeen in the NHANES sample. The Tsimane slope follows a similar pattern, but there is no apparent level period before the top of the childhood peak, which occurs around age eight. It may be that the shape has been compressed to the point that there is no level period. More likely the sample available simply lacks the resolution in early years to detect it.

Estimated Age at Peak IgE

Figure 4.3 and Figure 4.4 present the local regression models with minimum GCV values. However using only GCV to select a model can sometimes produce misleading results. Since our primary concern is the determination of peak IgE ages we examined the effect of model smoothing parameters on estimated peaks (Figure 4.6). In general, the choice of smoothing parameters had very little effect on the predicted peak ages. Models with low degrees of freedom sometimes predicted later peak ages for Shuar and NHANES and earlier peaks for Tsimane by effectively "cutting off" the peaks with over-smoothing. Models with sufficient degrees of freedom (>8) produced highly consistent results, predicting a peak for the NHANES sample between

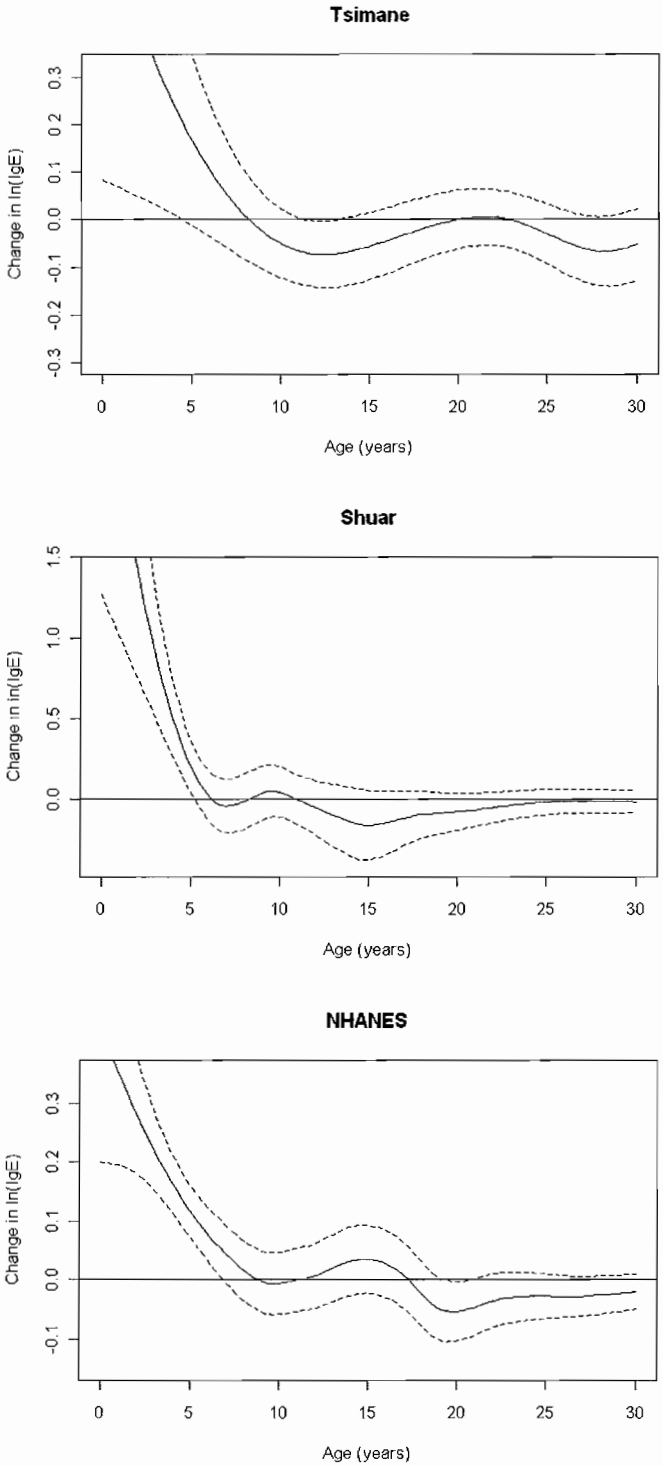

Figure 4.5. First derivative for ages 0 to 30 for the local regression in Figure 4.4.

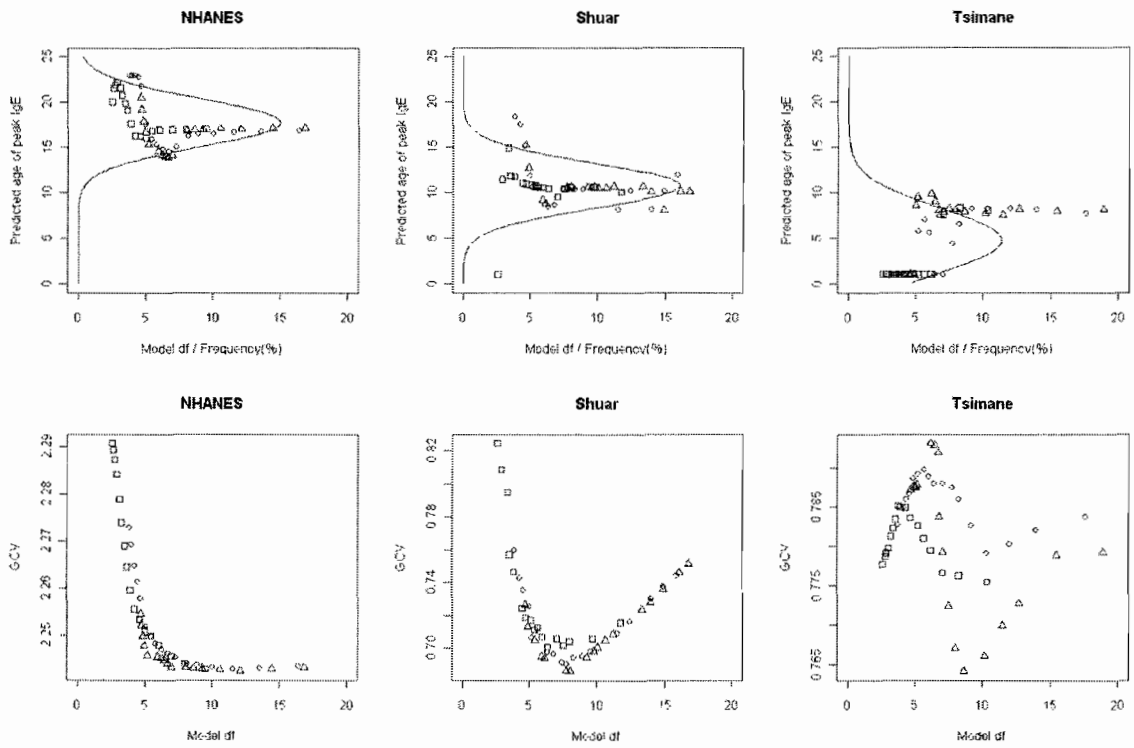

Figure 4.6. Relationship between model degrees of freedom, predicted age of peak IgE, and model GCV. Each point is a unique model with a one degree polynomial (squares), two degree polynomial (circles) or three degree polynomial (triangles). The normal distribution for each set of models is superimposed to aid interpretation.

ages 16 and 17, a peak for the Shuar sample between ages 8 and 10, and a peak for the Tsimane sample between ages 6 and 9.

We next examined the timing of the peaks relative to the lnIgE value at the peaks to determine whether they fit the predictions of the peak shift model. As Figure 4.7 illustrates, there is a significant linear relationship between peak age and peak value. Including all 153 loess model predictions in a linear regression suggests that peak age decreases 2.62 years (95% CI: 2.38-2.87) for every one unit increase in lnIgE with an

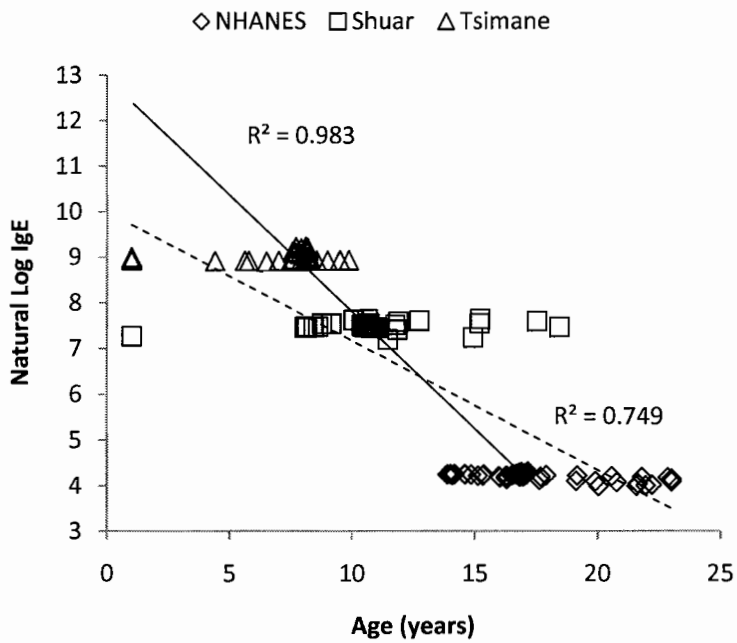

Figure 4.7. Correlation between age of peak lnIgE and value of peak lnIgE for all 153 models (dashed line, R^2=0.749) and for the five models for each sample with the lowest GCV values (15 total, solid line, R^2=0.983).

intercept at 29.07 years (model R^2 = 0.75, $F_{1,151}$ = 452.27, $p < .001$). However, a better fit and a slightly more conservative estimate are obtained from a linear model that includes only the five predictions for each population with the lowest GCV values. The low GCV model estimates that peak age decreases by 1.92 years (95% CI: 1.77-2.08) for each one unit increase in lnIgE, with an intercept at 25.03 years (model R^2 = 0.98, $F_{1,13}$ = 735.73, $p < .001$).

Are IgE Levels the Same at Birth?

Reports in the literature suggest that neonates produce very little IgE at birth, even in populations with high helminth prevalence (Bjerke *et al.,* 1994; Croner *et al.*, 1982;

Holt & Jones, 2000; King *et al.*, 1998). Although our samples do not include neonates, we wanted to determine whether the local regression models produced here are consistent with the expectation that IgE should be low at birth, and also to determine whether the models predict that neonates in all populations will have similar IgE values, despite the large differences between the samples at older ages. For Shuar and NHANES this is in fact the case. Predicted IgE at birth based on extending the local regression models is both low and not significantly different between the two populations (Figure 4.8).

Predicted lnIgE for NHANES at birth is 2.71+/- 0.29 (S.D.), and for Shuar is 2.26+/-1.82(S.D.). However for Tsimane, predicted lnIgE at birth is 7.41 +/- 1.46, suggesting that our model may not be capturing the slope of the initial increase. To further test the predicted shape at birth, we ran linear models on only the children age six

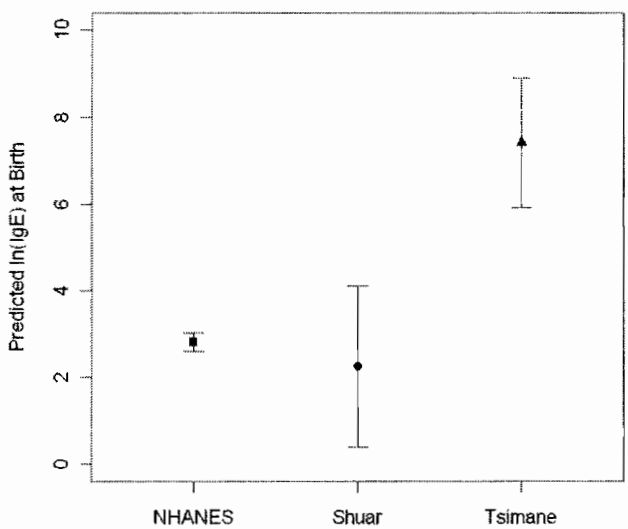

Figure 4.8. Predicted IgE at birth according to the local regression fit shown in Figure 4.4. Error bars are the local 95% confidence interval for the mean prediction.

and younger, before the peak in IgE in any of the populations. We first ran models with only Shuar and Tsimane (Table 4.5). Using linear terms, the quadratic model with a shared intercept at age zero was significantly better than any of the others. However, since IgE increased rapidly at first but then at a decreasing rate we suspected that using lnAge might provide a better model fit, as others have found (Wahyuni *et al.*, 2005). This proved to be the case, with the optimum model including only terms for ln(Age+1) x sample plus a shared intercept (Age +1 was used so that the intercept would be at age zero instead of one, and in fact provides a better fit than lnAge) (Table 4.5). We next added Tsimane to the models to test whether the model would predict a shared intercept

Table 4.5. Comparison of linear models with NHANES and Shuar only

Model	Parameters	Res Df	RSS	Δ Df	Δ SS	F	Pr(>F)	
A1	Age	1132	2830.5					
A2	Sample	1132	2565.0	0	265.47			
A3	Age x Sample	1131	2435.8	1	129.23	60.37	<.001	***
A4	Age x Sample + Sample	1130	2423.9	1	11.93	.57	.018	*
A5	Age x Sample + Age^2 x Sample	1129	2414.7	1	9.21	.30	.038	*
A6	Age x Shuar + Age^2 x Shuar + Shuar	1128	2414.4	1	.24	.11	.740	
B1	ln(Age+1)	1132	2825.6					
B2	Sample	1132	2565.0	0	260.51			
B3	ln(Age+1) x Sample	1131	2416.3	1	148.78	69.52	<.001	***
B4	ln(Age+1) x Sample + Sample	1130	2416.1	1	.14	.06	.802	
B5	ln(Age+1) x Sample + $ln(Age+1)^2$ x Sample	1129	2415.5	1	.63	.29	.589	
B6	ln(Age+1) x Sample + $ln(Age+1)^2$ x Sample + Sample	1128	2414.2	1	1.33	.62	.431	
B3	ln(Age+1) x Sample	1131	2416.3					
A5	Age x Sample + Age^2 x Sample + Age^2 x Sample	1129	2414.7	2	1.59	.37	.690	

*** <.001 ** <.01 *<.05 All models include an intercept term.

Table 4.6. Linear models including all three groups.

Model	Parameters	Res Df	RSS	Δ Df	Δ SS	F	Pr(>F)
C1	Model B3 + ln(Age+1) x Tsimane	1160	2441.2				
C2	Model B3 + Tsimane	1160	2436.5	0	4.650		
C3	Model B3 + ln(Age+1) x Tsimane + Tsimane	1159	2435.8	1	.730	.347	.556
	Model C3 vs. Model C1	1159	2435.8	1	5.380	2.558	.110

Table 4.7. Model parameters for the optimum model (C2)

	Estimate	SE.	t	Pr(>|t|)	
(Intercept)	2.525	.143	17.67	<.001	***
Tsimane	6.315	.300	21.04	<.001	***
ln(Age) x Shuar	2.613	.152	17.18	<.001	***
ln(Age) x NHANES	.786	.100	7.82	<.001	***

*** <.001 ** <.01 *<.05
Residual standard error: 1.449 on 1160 degrees of freedom
Multiple R-squared: 0.3648, Adjusted R-squared: 0.3632
F-statistic: 222.1 on 3 and 1160 DF, p-value: < .001

at age zero for Tsimane as well. However, for the optimum model did not predict a shared intercept for Tsimane. Instead the model with only the constant value for Tsimane fit best (Table 4.7). Both models are shown in Figure 4.9.

Does IgE Decline with Age?

Finally, we tested whether IgE shows significant changes with advancing age. An increase in IgE might be expected if there is a consistent accumulation of IgE producing clones with age. A decrease might be related to immunosenescence. Within the confines

of the sample sizes available, IgE levels were remarkably stable in all three populations. Based on the loess fit lines, we tested whether IgE declines after age sixty in the NHANES sample. We found that IgE does show a consistent slight decline, but only for females (Females: $\beta = -.028$, $F_{1,675} = 16.18$, $p < .001$, Males: $\beta = -.007$, $F_{1,734} = .92$, $p = .339$). There was no significant decline in the Tsimane population and insufficient sample for this age range in the Shuar sample. The Shuar sample shows an intriguing increase after about age forty-five, perhaps interpretable of evidence that helminth levels were higher for Shuar in the recent past. However this increase is non-significant with the sample available.

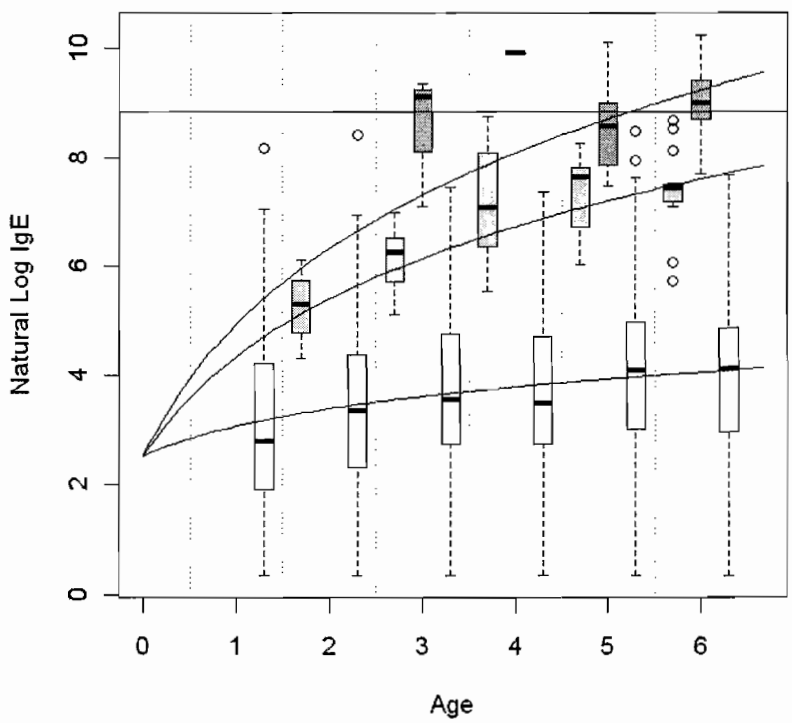

Figure 4.9. Boxplots for lnIgE in NHANES (white), Shuar (light grey) and Tsimane (dark grey) by year and fit lines from models C1 and C2. Note that the fit lines are aligned with the center of each age category, not with the boxplots.

DISCUSSION

We report on the age patterning of IgE in three populations: U.S. residents, Ecuadorian Shuar, and Bolivian Tsimane. Overall, Tsimane were found to have the highest IgE levels, with a geometric mean of 6,298 IU/ml, consistent with their high degree of helminth infection (Tanner *et al.*, 2009). At 1,196 IU/ml, Shuar levels were exceptionally high by U.S. standards, but not necessarily in comparison with other indigenous populations. NHANES levels were 52 IU/ml.

As we noted above, one potential limitation on the comparison between these populations is that different methods were used to determine IgE levels. For certain analytes dried blood spots yield results that are lower than those obtained for serum, primarly due to degradation or denaturation of blood proteins with drying (e.g., Shirtcliff *et al.*, 2001). However, this does not appear to be the case for IgE or other immunoglobulins which degrade very little (Terhell *et al.,* 1996; 2000; 2001; Stapel *et al.,* 2004; Tanner & McDade 2007). Apart from degradation, the primary source of variation in results from serum versus dried blood spots lies in the dilution factor used to match the eluted blood spots with standards or matched serum. Without the appropriate dilution, blood spot results will still be highly correlated with serum results but will be off by a constant factor. In this study we avoid this problem as much as possible by creating blood spot standards by mixing serum standards with equal parts washed erythrocytes and spotting onto paper (Tanner & McDade 2007). Although not perfect, this procedure creates standards that yield results that vary from serum values by no more than ten or fifteen percent (e.g., McDade *et al.*, 2004). In short, the dried blood spot results obtained

here may be off from serum values by some small factor, but are unlikely to be off by the order of magnitude differences we see between these populations.

For further comparison, we reviewed IgE levels for populations around the world (Table 4.8). The review shows that the three populations included in this study represent the range of population mean IgE values reasonably well. Moreover, the values lie within the expected ranges for similar populations. The Tsimane values resemble those of other South American groups with low levels of acculturation. The Shuar values are similar to other South Americans living in poor but somewhat acculturated areas, such as the poor areas of Venezuela (Hagel *et al.,* 1993; 1995), an Amazonian town to the north of the Shuar territories (Kron *et al.,* 2000), and a poor area outside of Quito (Cooper *et al.,* 2008). We therefore have no reason to suspect that the use of different methods of IgE determination has created any substantial bias in the results for these three populations.

Although many studies have reported elevated IgE levels in populations infected with parasites such as helminths and malaria, very few have carefully characterized the age patterning of IgE, and none that we are aware of have tested for a peak shift. In this study we have used local regression to describe the age patterning in three populations and found clear evidence for a shift in the age of peak IgE. The association between peak IgE level and peak age is remarkably linear, each one unit increase in the natural log of IgE lowering the peak age by about two years, from about age seventeen in the U.S. to about age eleven in the Shuar and age eight in the Tsimane. The shift we observe is

consistent with mathematical models of helminth infection and acquisition of immunity (Anderson & May, 1985; Woolhouse, 1992; Woolhouse, 1998).

It may be that detection of this peak shift is facilitated by the fact that the Shuar and Tsimane live in similar environments in the Amazon basin of South America. The review in Table 4.8 shows significant geographical patterning in IgE levels, with the highest levels found among lowland South American populations living in the Amazon basin. This is not surprising, given that a moist, tropical environment is ideal for helminth transmission. However, other parasites, such as *P. falciparum*, also raise total IgE levels, as is evidenced not just by association but by the presence of anti-plasmodial IgE (Perlmann *et al.,* 1994; Perlmann *et al.*, 1997; Perlmann *et al.*, 1999). (In fact, *Ascaris* infection may provide some protection against malaria, perhaps by encouraging T_H2 response (Nacher *et al.*, 2000).) We would expect IgE levels due to malaria to follow a different pattern since the life cycle of malarial plasmodiums is significantly different from that of helminths. However, malaria is unlikely to be an important factor for the populations studied in this paper. Although malaria is present in parts of the Shuar territory, it is not present in the village where the data for this paper was collected, and very few individuals in the village report ever having had malaria. Malaria also appears to be absent from the Tsimane territories, with no Tsimane reporting malaria in extensive health interviews.

Table 4.8. Review of IgE levels by population as reported in the literature

Region	Population	G. Mean (IU/ml)	Predicted Peak Age	Reference	Sample	n	Ages
S.A.	Multiple indigenous groups, Venezuela	13,088	7	Lynch *et al.*, 1983	Serum	274	18.5±13.6
S.A.	Waorani, Ecuador	10,153*	7	Kaplan *et al.*, 1980	Serum	227	all ages
S.A.	Dicuron (Waorani), Ecuador	10,572*	7	Kron *et al.*, 2000	Serum	31	15-75
S.A.	Waorani, Ecuador	9,806	7	Buckley *et al.*, 1985	Serum	229	all ages
S.A.	Warao, Venezuela	7,004	8	Hagel *et al.*, 2006	Serum	159	8.6±2.5
S.A.	**Tsimane, Bolivia**	**6,298**	8	**This study**	**Serum**	**329**	**3 to 84**
S.A.	Dicuron (Waorani), Lago Agrio, Ecuador	4,143*	9	Kron *et al.*, 2000	Serum	8	adults?
Asia	Indonesia	3,162	10	Terhell 2002	DBS	167	0 to 10 and adults
Asia	Tibetan (living in Nepal)	2,930	10	Buckley *et al.*, 1985	Serum	39	all ages?
Asia	Indonesian	2,570	10	Wahyuni *et al.*, 2005	Serum	466	5 to 84
S.A.	"Slum" of Caracas, Venezuela	2,423	10	Hagel *et al.*, 1993; 1995	Serum	85	8.5±2.5
Africa	Liberia	2,123	10	Perlmann *et al.*, 1994	Serum	57	adults
S.A.	**Shuar, Ecuador**	**1,196**	11	**This study**	**DBS**	**163**	**2 to 67**
S.A.	Quichua, Ecuador	1,189*	11	Kron *et al.*, 2000	Serum	16	adults?
S.A.	Brazil	1,047	12	Grant *et al.*, 2008	Serum	822	26.9±18.7
S.A.	Pichincha, Ecuador	1,004	12	Cooper *et al.*, 2008	Serum	1,632	grades 2 to 7
Africa	Ethiopian Born (1-3 months in Israel)	1,016*	12	Iancovici Kidon *et al.*, 2005	Serum	11	13.7±1.0
Africa	Ethiopian Born (One year in Israel)	1,292*	11	Iancovici Kidon *et al.*, 2005	Serum	11	14.7±1.0
Africa	Nigeria	973	12	McSharry *et al.*, 1999	Serum	92	5 to 15
Africa	Gambia (Rural school children)	962	12	Godfrey, 1975	Serum	131	schoolchildren

Table 4.8. (continued)

Region	Population	G. Mean (IU/ml)	Predicted Peak Age	Reference	Sample	n	Ages
Asia	Thailand	647	13	Perlmann *et al.*, 1994	Serum	23	adults
S.A.	Non-parasitized school children, Venezuela	450	13	Hagel *et al.*, 2006	Serum	70	7.6±2.5
Africa	Tanzania	397*	14	Perlmann *et al.*, 1999	Serum	230	0 to 29
Africa	Gambia (Urban school children)	368	14	Godfrey, 1975	Serum	60	schoolchildren
Africa	Gambia (Rural)	364	14	Nyan *et al.*, 2001	Serum	142?	> 15
Africa	Gambia (Urban)	332	14	Nyan *et al.*, 2001	Serum	142?	> 15
Africa	Madagascar	301	14	Perlmann *et al.*, 1994	Serum	54	2 to 35
Africa	Ethiopian Born (>7 years in Israel)	135*	16	Iancovici Kidon *et al.*, 2005	Serum	10	14.7±1.0
N.A.	North Carolina, U.S.A. (White and Black)	108	16	Buckley *et al.*, 1985	Serum	84	18-35
Europe	Croatia	107[c]	16	Dodig *et al.*, 2006	Serum	7,975	0 to 16
M.E.	Ethiopian Israeli Born	54*	17	Iancovici Kidon *et al.*, 2005	Serum	15	6.4±2.3
Europe	Greek	54[c*]	17	Petridou *et al.*, 1995	Serum	484	1 to 14
N.A.	**U.S.A. (Multiple Ethnicities)**	**52**	17	**This study**	**Serum**	**8,336**	**1 to 85**
N.A.	Canada (only non-allergic)	12	20	Holford-Strevens *et al.*, 1984	Serum	1,814	20-65
Europe	Sweden (only non-atopic)	8	21	Perlmann *et al.*, 1994	Serum	38	not given

* the published arithmetic mean was converted to geometric mean under the assumption of a lognormal distribution using: $G.M. = e^{\left(\ln(\bar{x}) + \frac{1}{2}\ln\left(1+\left(\sigma^2/\bar{x}^2\right)\right)\right)}$ where $\bar{x}$ is the arithmetic mean and σ is the standard deviation.

[c] Two or more reported groups were combined to form a single population estimate by converting to log IgE, calculating sample size weighted average log IgE and then converting back to geometric mean.

Region abbreviations: S.A. = South America, N.A. = North America, M.E. = Middle East

A number of studies have noted that IgE is very low at birth, but increases rapidly in the first five years of life (Grundbacher, 1975; Johnson *et al.*, 1998; Lindberg & Arroyave, 1986; Petridou *et al.*, 1995). Most of these studies have been conducted in North America or Europe, and most report that IgE is relatively stable after age five or six. As our NHANES results indicate, increases after this point are slight and gradual which likely explains why many studies have failed to remark of future increase.

Few other studies have reported on age patterns in total IgE, and those that have report only on five or ten year age categories, making identification of peaks difficult. For example, Buckley et al (1985) report that IgE was highest among Waorani in 10-20 year olds (10,797 IU/ml). While this is somewhat higher than the levels reported for older age groups (7,848-9,760 IU/ml) it is only slightly lower in those zero to ten (10,227 IU/ml), meaning the true peak could lie anywhere within that range. For comparison, we have used the model obtained in this study to predict peak IgE levels for the other populations in Table 4.8. The model predicts a peak around seven years for the Waorani.

Reporting on a malarial region in Tanzania, Perlmann et al (1999) indicate a peak in IgE in 11-15 year olds, with an estimated geometric mean for the sample of 397 IU/ml. Despite the fact that the authors attribute the increase in IgE to malaria, the value is consistent with our prediction of a peak at 14 years of age given the population IgE level.

One of the few studies to report detailed age profiles (Dodig *et al.*, 2006) reports on children in Croatia with unexceptional IgE levels (geometric mean about 100 IU/ml). As many studies examining IgE do, this study was focused on allergies and so separated children into atopic and non-atopic based on skin prick response to allergen. In this

study, non-atopic children showed an initial increase to age nine, a slight decrease, and then a second peak at age fifteen, consistent with the predicted population peak at age sixteen. The shape of the increase, with an initial peak and then a second peak, is also remarkably similar to the age profiles seen in this study for the NHANES and Shuar sample. For atopic children with an overall geometric mean of about 300 IU/ml, the peak was less clear, occurring sometime between age 10 and 16. However, we should be careful about confusing increases in IgE due to allergy with those due to helminths, as it is not at all clear that they should have the same pattern.

A few studies have also noted age-related declines in total IgE. Wahyuni, et al (2005) in a study conducted in Indonesia, report a geometric mean IgE level of 3,467 IU/ml in those under age fourteen, decreasing to about 1,950 in those over age 44. Overall, the authors note that they found that the natural log of age fit best in regression models to control for age, just as we found in this study. However, they do not report further details.

Helminth infections themselves show significant age patterning consistent with the IgE peaks reported in this study. Typically, infection peaks just before or during adolescence (Hotez *et al.*, 2008). In southern Venezuela, *Trichuris trichiura* and roundworms peak between the ages of 7 and 12, *Ascaris* peaks between 7 and 10, and hookworms between 13 and 18 (Hurtado *et al.*, 2008). In contrast, among the Tsimane, hookworm peaks between 6 and 9 (Hurtado *et al.*, 2008). In Camaroon, *Trichuris* peaks at age seven (Faulkner *et al.*, 2002). In a high transmission area in Zimbabwe,

Schistosoma haematobium infections peak between the ages of five and nine, whereas they peak between 10 and 14 in lower transmission areas (Woolhouse, 1998).

In addition to the peak ages reported in this study, the shape of the age patterns presented may have additional implications for understanding helminth transmission and immune response. Woolhouse's original models predict that the mean level of resistance in a population will fall slightly in ages older than the initial peak age when antigenic stimulus is provided by adult parasites, rather than larval parasites (Woolhouse, 1992). We see such a decrease in the Shuar and perhaps NHANES samples, with a much more modest decrease in the Tsimane sample. A critical role for adult parasites in generating an antibody response is also consistent with the many years of exposure required to develop resistance to helminths (Woolhouse & Hagan, 1999). There are several possible explanations for the sharp decrease among Shuar but not Tsimane. It may be that Shuar are exposed to a lower diversity of parasites than the Tsimane (Galvani, 2005), that the Shuar are primarily infected with different species than the Tsimane, or that there are differences in immunological memory between the two populations, perhaps due to overall pathogen levels, nutritional factors, or even genetic propensities.

In addition to understanding the immunoepidemiology of helminths, understanding how IgE levels are impacted and develop in diverse circumstances may aid our understanding of how the immune system evolved and may be affected by modern environments. A number of studies have shown an inverse relationship between allergic disease and helminth infection (Yazdanbakhsh & Wahyuni, 2005; Yazdanbakhsh *et al.*, 2002). Although there are a number of hypothesis for the exact mechanisms underlying

the relationship between allergy and helminths, recent work points to a role for regulatory T cells activated by infection (Maizels & Yazdanbakhsh, 2003; Maizels, 2005), or perhaps changes in inflammatory cytokines (Yazdanbakhsh *et al.*, 2002). What remains unclear is exactly how changes in the immune system, and in particular the T_H1/T_H2 balance, are regulated and develop, and moreover, whether these changes are malleable or whether there are critical periods that set lifetime patterns. Understanding these changes is critical for addressing diseases in the developed world, such as allergy, as well as for addressing the health problems facing indigenous populations. If a T_H2-biased immune system is more susceptible to infections that require a T_H1 response, then the true impact of helminths on global health may be much greater that commonly thought (Hurtado *et al.*, 2004).

BRIDGE TO CHAPTER V

In this chapter I described in detail the age patterning of IgE in the Shuar and two other groups. Compared to levels in the United States, the Shuar have incredibly high levels of IgE, indicative of a high prevalence of helminth infection. The next chapter examines IgE in relation to C-reactive protein, a marker of inflammation, and growth. Chapter V returns to the questions introduced throughout the other chapters in this dissertation. Life history theory predicts tradeoffs between the demands of growth, maintenance, and reproduction, as well as trade-offs within each of these categories (Figure 1.1). Chapter V examines trade-offs between IgE and growth, returning to the

question from Chapter II of why Shuar have a high prevalence of stunting. Chapter V also examines the effects of family members on growth and IgE, and the trade-off between growth and IgE, using the modeling techniques developed in Chapter III. Finally, Chapter V presents a unified model for the effects of family members on life history trade-offs between growth and multiple branches of immune function.

CHAPTER V

ARE QUANTITY-QUALITY TRADE-OFFS REFLECTED IN THE IMMUNE FUNCTION OF HUMAN CHILDREN?

This chapter is co-authored with J. Josh Snodgrass, Felicia C. Madimenos, Melissa Liebert, and Lawrence S. Sugiyama. Snodgrass, Madimenos, Liebert, and Sugiyama were all central members of the team that collected the Ecuadorian data. Josh Snodgrass made his lab available for analyses and provided critical expertise in the analysis of dried blood spots. Lawrence Sugiyama is director of the Shuar Life History project and as such directed the fieldwork upon which this chapter is based. The author of this dissertation proposed the work contained, obtained funding, and collected samples in Ecuador. The analyses, writing, and figures contained in this chapter are the work of the author of this dissertation.

INTRODUCTION

The costs of responding to and defending against pathogens are often underappreciated in life history models. Life history theory typically divides the allocation of energy into somatic maintenance, growth, and reproduction, but frequently focuses on reproduction and growth as the principal determinants of optimal life history solutions (e.g., Charnov, 1991; Hagen & Barrett, 2009; Hill & Hurtado, 1996; Hrdy, 2009; Kramer *et al.*, 2009; Reiches *et al.*, 2009; Trivers, 1972). This is surprising given the costs of immunity. Fever is estimated to increase metabolic rate by 13% for every degree increase in body temperature, while sepsis or systemic infection can increase

metabolic costs by 50% (Lochmiller & Deerenberg, 2000). Protein synthesis increases during an immune response, from about 3.5g to 6g of protein per day per kilogram of body weight (an estimated expense of 285 kcal/day) (McDade, 2003). This increase in protein synthesis requires not just energy, but amino acids sometimes only obtainable from dietary sources. Specific types of immune defense are also regulated by nutrient availability; for example, Vitamin A seems to increase the response of T_H1 helper T-cells (Long & Nanthakumar, 2004). For humans, periods of illness during childhood can result in growth delay and stunting (Bogin, 1999; McDade *et al.*, 2008; Victora, 1992). This pattern is common across species, where mounting an immune response have bas been shown to decrease growth, survival, and reproduction (Demas, 2004; Klein & Nelson, 1999; Sheldon & Verhulst, 1996; Uller *et al.*, 2006).

In addition to the short term costs of mounting an immune response, the dynamics of pathogen transmission have a significant impact on life histories (Nunn & Altizer, 2006). For example, cohorts experiencing decreased childhood mortality and decreased exposure to infectious disease also experience greater adult longevity and height (Crimmins & Finch, 2006). The dynamics of pathogen transmission are also important because there may be patterns in the ages at which individuals are affected by parasites, which entail different, age specific costs and thus have differential effects on life histories (Woolhouse, 1998; Chapter IV). Pathogen transmission is affected by factors such as population densities, household crowding (Baker *et al.*, 2000), sexual contact (Low, 1990; Nunn *et al.*, 2000), food sharing, and grooming (Loehle, 1995). Thus, there is a reciprocal relationship between pathogen dynamics and life history allocations such as

the rate of reproduction, the investment given to offspring, and the strength of immunity in the local population.

One of the most fundamental trade-offs faced by organisms is the trade-off between producing many offspring and investing less in each, or producing fewer offspring so that each can receive a greater share of investment (Clutton-Brock, 1991; Lack, 1947; Trivers, 1972; Williams, 1966). Typically this trade-off in formulated in terms of the energetic costs. However, there may be other costs associated with producing many offspring, such as increases in pathogen transmission. Concordantly, parents and alloparents may provide non-energetic benefits if they reduce pathogen burden through grooming, carrying, cooking, and so on.

Among humans, the trade-off between quantity and quality of offspring has found limited empirical support using measures of quality such as growth, survival, and recruitment into the breeding pool (Blurton Jones & Nicholas, 1986; Gillespie *et al.*, 2008; Hagen *et al.*, 2006; Larrea & Kawachi, 2005; Chapter II). However, trade-offs should also be apparent using other markers of quality, such as investment into immune defense. Moreover, if family size affects pathogen transmission, then family size is also predicted to affect the relative allocation of resources between multiple markers of quality, such as immune function and growth.

Ecological Immunology

Although quantity-quality tradeoffs in immune function have not been examined, a number of studies have examined how immune function responds to ecological and

social variables, a field of study referred to as *ecological immunology* (McDade & Worthman, 1999; McDade, 2003; Sheldon & Verhulst, 1996). Each of the several different types of immune defense has its own energetic costs and benefits. These include innate (non-specific) immunity, cell-mediated immunity, and humoral immunity. Energy must be allocated between competing immunological pathways at all levels of this hierarchy (Campbell *et al.,* 2001; Long & Nanthakumar, 2004; McDade, 2003; McDade, 2005). This is clear when the effects of energy availability are examined. Obesity increases inflammation and may also contribute to increased allergy (Hersoug & Linneberg, 2007). In contrast, children who are malnourished often show reduced immune response, making vaccines less effective. At the same time, malnourished children may allocate greater *relative* amounts of energy towards immunity. Azevedo *et al.* (2005) found that the white blood cells of malnourished children grown in culture actually produced greater TNF-α (a marker of inflammation) and required less bacterial protein to stimulate TNF-α production. These same children had lower TNF-α *in vivo*, where energy was limited, but higher responses *in vitro*, where energy was no longer limiting.

Variables studied in ecological immunology reflect not just environmental demands (e.g., defending against helminths vs. defending against viral infections) but also what might be thought of as *immune strategies*. In addition to the energetic costs, certain types of immune response may entail additional costs. For example, inflammation is a non-specific immune defense that will help clear a pathogen but is more likely to cause collateral damage due to oxidative stress than cell-mediated or

humoral immunity. Inflammation also increases long-term risk of chronic diseases such as atherosclerosis and cardiovascular disease (Pearson *et al.,* 2003; Ridker *et al.*, 1998). Different immune responses also have different time costs. If an organism has low energy stores or high extrinsic mortality risk, prolonged inactivity and illness can limit mating opportunities or result in fatal energy shortages. Thus, defenses which can quickly clear a pathogen, such as inflammation, may be preferred. In longer living organisms with low mortality risk and sufficient energy stores for prolonged immune activation, defenses that limit collateral damage may be preferred, even if they take longer to achieve pathogen clearance (Martin *et al.*, 2008). For these organisms, investing in the future may take precedence over investing in the present.

The Present Study

In this paper we report on three studies that examine trade-offs between growth, inflammation, and humoral immunity. The studies were all conducted amongst the Shuar, an Amerindian group from lowland Ecuador. In the first study we examine tradeoffs between immunoglobulin E (IgE), a humoral response to helminth infections, C-reactive protein (CRP), a marker of inflammation, and growth in Shuar children. Both IgE and CRP are elevated in Shuar in comparison to samples from the United States and Europe (Chapter IV). However, we predict that these branches of immunity will trade-off against one another.

In the second study we examine trade-offs between body size, IgE, and CRP in Shuar adults, to test the hypothesis that allocations set in childhood will persist into

adulthood. Other studies have found trade-offs between fat free mass and CRP (Lassek & Gaulin, 2009). We know of no published research that has examined associations between IgE and body mass.

Finally, the third study examines the effects of family members on IgE, CRP, height and weight, and the trade-offs between these measures. We test three hypotheses derived from life history theory. First, we predict that additional adults in the household will be associated with increases in growth markers due to increases in the household energy pool. Second, we make two predictions about how additional children in the household will affect growth and biomarkers. We predict that controlling for energy availability we will find evidence for a quantity-quality trade-off in both growth and immune function, with IgE, height, and weight all predicted to be lower in households with more dependents. However, we also predict that an increase in dependents will cause a shift in energy away from growth and towards immune response, as a consequence of increased disease exposure. Since these two hypotheses predict opposite effects on IgE, but the same effect on growth, we predict that the effect of children on growth will be greater than the effect on IgE.

METHODS

Markers of Immune Function

Immunoglobulin E. Intestinal helminths such as *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm and *Strongyloides stercoralis* infect approximately a billion people worldwide (Hotez *et al.,* 2008; Hurtado *et al.*, 2004; Hurtado *et al.*, 2008; Stephenson *et*

al., 2000). Helminth infections are associated with a general shift in the host immune system towards a T_H2 biased phenotype, characterized in particular by increased production of immunoglobulin E (IgE) (Maizels & Yazdanbakhsh, 2003; Maizels, 2005). Overall Shuar have relatively high IgE levels, particularly in comparison to North American and European populations (Chapter IV). Although helminths are associated with malnutrition and growth stunting on a population level (Blair Trujillo *et al.,* 2003; Stephenson *et al.*, 2000), documenting associations on an individual level has proven difficult (Tanner *et al.*, 2009). In this study we measure IgE as both as a marker of investment into humoral immunity and as an indicator of past exposure to helminths to examine how these trade-off with growth and are influenced by household composition.

C-reactive protein (CRP). CRP is a nonspecific acute phase reactant that rapidly increases in plasma concentration in response to inflammation, infection, and injury (Pepys & Hirschfield, 2003). Research has linked elevated levels of CRP to factors such as age, obesity, and smoking (e.g., Danesh *et al.,* 1999; Hutchinson *et al.*, 2000; Rexrode *et al.*, 2003; Visser *et al.*, 1999). More recently, a number of studies have documented associations between elevated CRP concentrations and several dimensions of psychosocial stress, including perceived stress (McDade *et al.*, 2006), fear of terror (Melamed *et al.*, 2004), lack of social integration (Ford *et al.*, 2006), depression (Danner *et al.,* 2003; Ford & Erlinger, 2004), and depressive symptoms (Dressler *et al.,* 2006; Penninx *et al.*, 2003; Suarez, 2004). Further, CRP has been found in a number of studies to be inversely correlated with socioeconomic status, such that lower socioeconomic

status is linked with higher CRP concentrations (Gimeno *et al.,* 2007; Nazmi & Victora, 2007): individuals living at or below the poverty line are more likely to have extremely high CRP concentrations (Alley *et al.*, 2006). CRP levels were also elevated among Tsimane children with greater exposure to pathogens (McDade *et al.*, 2005), and associated with poorer growth (McDade *et al.*, 2008). In terms of life history tradeoffs, CRP is a marker of investment in non-specific immune defenses (McDade, 2003). CRP can also indicate active infections, since levels become elevated in response to infection and drop about a week after infection (Pearson *et al.*, 2003).

Ethnographic Context

Shuar are Amerindians from the Amazonas region of Ecuador, closely related to other groups such as the Achuar and Shiwiar who belong to what has been known as the Jivaroan language group (Descola, 1994; Descola, 1996; Harner, 1984). Traditionally, Shuar lived in scattered clusters of a few households, their economy based on horticulture, hunting, and fishing. Our previous work has shown that approximately 40% of Shuar children are stunted, and that Shuar are much more likely to be stunted than both the closely related Shiwiar and Achuar, as well as non-indigenous children living in the same area (Blackwell *et al.*, 2009). Although we know of no studies examining helminth infections in the Shuar, per se, recent studies report infection rates of around 50% in other Ecuadorian populations, with *Ascaris* the most prevalent parasite. These include children in rainforests villages on the western side of the Andes (Sackey *et al.,* 2003) and Napo

Runa children from the Rio Napo area in northwestern Amazonas (San Sebastian & Santi, 1999; San Sebastian & Santi, 2000).

The data for this study was collected by ADB, JJS, FCM, and LSS as part of the Shuar Life History Project (www.uoregon.edu/~sugiyama/shuar) in a village of approximately 500 people, located approximately 45 minutes by truck from the town of Sucúa, Ecuador. The dirt road to the village has only been improved in the last few years, before that the village was reached only on foot. No one in the village owns a car, but a truck comes through about once a day to offer travel to Sucúa (providing service much like a bus). Many adults travel to Sucúa once every week or two. Since 2000, the village has had a health clinic staffed by an auxillary or nurse that provides vaccinations and dispenses basic medications such as albendazol for parasites, and antiboiotics, acetaminophen, and vitamins for most everything else. The village also has a primary school, which most children attend. There is a water line that pipes untreated water from a spring through the central part of the village, and houses along this central road have spigots. Other houses obtain water either from their neighbors or from nearby streams. We collected household inventories which show that about 80% of households get their water from the water line. About 70% of households have outhouses (almost all without water), the rest typically use the forest and other open spaces. Electricity arrived in 2000 and 45% have electricity which can be used for multiple purposes, while 20% have electricity only for light, and 30% have no electricity.

All participants gave informed consent or assent, with both parental consent and child assent for subjects under fifteen. The study was approved by the village leaders, the

Ministerio de Salud Pública de Morona Santiago, the Federacíon Interprovincial de Centros Shuar (FICSH), and the Institutional Review Board of the University of Oregon.

Anthropometry, Blood Collection, and Analysis

Stature was recorded to the nearest 1.0 mm using a field stadiometer (Seca Corporation, Hanover, MD). Body weight was measured in light clothing (without shoes) to the nearest 0.1 kg using a Tanita BF-558 electronic scale (Tanita Corporation, Tokyo, Japan). Blood samples were collected following standard procedures to collect dried blood spots (McDade *et al.*, 2007). Briefly, a finger prick using a sterile, disposable lancet was used to obtain three to five 50μL drops of whole capillary blood spotted onto standardized filter paper (No. 903; Whatman). Blood spot samples were dried for four hours and then sealed in airtight bags and frozen in the village clinic freezer for one to three weeks. Blood spots were kept cold with freezer packs for transport to the Ecuadorian capital, Quito. They were allowed to come to room temperature for transport by plane to the University of Oregon (approximately 12 hours), after which they were stored at -30°C until analysis.

IgE levels were determined by ELISA following a commercially available protocol (Bethyl Labs, Inc.: #E80-108 and #E101) adapted for use with blood spots (Tanner & McDade, 2007). We have described methods for IgE previously (Chapter IV). CRP levels were determined by high sensitivity ELISA following a published protocol (McDade *et al.*, 2004) modified for use with different coating and detection antibodies since the antibodies from the original protocol are no longer available in the U.S. The

modified protocol has been validated against both the published protocol and against blood plasma samples (T. McDade, personal communication). Blood spot standards were prepared by serial dilution of Dade Behring N Rheumatology Standard SL (#OQKZ) in dilution buffer (0.01 M phosphate buffer, 0.145 M NaCl, ph 7.2, 5g/L BSA). Diluted standards and controls (BioRad Liquichek Cardiac Markers Plus #180X) were then mixed with an equal volume of washed erythrocytes and spotted onto filter paper cards (Whatman #903). Spots were allowed to dry overnight at room temperature and then frozen at -30°C. Mouse monoclonal antihuman CRP detection antibody (Biodesign #M86284M) was biotinylated with the EZ-Link Sulfo-NHS-LC biotinylation kit (Pierce #21435) according to the supplier's directions.

The night before the assay a 3.2 mm disc was punched from each standard, control, and unknown and eluted overnight in 250 µl assay buffer (0.01 M phosphate buffer, 0.5 M NaCl, 0.1% Tween 20). 96-well plates were coated with 100 µl mouse monoclonal anti-human CRP coating antibody (Biodesign #M86005M) diluted to 2 µg/ml in coating buffer (0.01 M phosphate buffer, 0.145 M NaCl, ph 7.2). Plates were rotated for 15 minutes and then incubated overnight at 4°C. In the morning plates and samples were removed from the refrigerator and allowed to come to room temperature, with samples rotating at 300 rpm for 1 hour. Plates were washed 4x with a BioTek ELx50 strip washer and then soaked for 30 minutes with 350 µl assay buffer. Assay buffer was aspirated and 100 µl of each eluted standard, sample, and control was added to plate wells in duplicate. The plate was covered and rotated at 250 rpm at room temperature for 90 minutes. Wells were then washed 4x with assay buffer and 100 µl

diluted biotinylated detection antibody (final concentration: 5 ng/ml) was added to each well. The plate was rotated for 90 minutes and then washed 4x. 100 µl diluted (1:7500) streptavidin-HRP (Biodesign #V8Z21-2712) was added to each well and incubated for 30 with rotation. The wells were washed 4x and 100 µl prepared chromogenic substrate (DAKO OPD #S2045, H_2O, H_2O_2) was added and incubated for 30 minutes at room temperature. The reaction was stopped with 100 µl 0.5 M sulfuric acid. After 5 minutes the plates were read at 490 nm on a Biotek ELx808 plate reader and a four parameter fit was used to generate a standard curve from the standards. CRP values were converted to plasma equivalent values using the parameters from the protocol validation (T. McDade, personal communication): $CRP_{plasma} = 2.36 \times CRP_{dbs} + 0.39$.

Age Estimation

Approximate birthdates were available for most Shuar children. In general, these birthdates are accurate to the month, particularly for children born after the health clinic was established in the study village in 2000. For adults ages were less accurate, particularly for individuals older than about forty. Many had birth dates on their government identification (by law all Ecuadorians are required to register for identification). These were used but were crosschecked with extensive genealogical information collected on individuals in the village. Geneologies included siblings and offspring, given in order of birth. Overlapping genealogies were collected from multiple informants in order to cross-check information.

Age Standardized Variables

Since height, weight, BMI, weight-for-height (WFH), IgE, and CRP all vary with age, for some analyses least squares models were fit to each parameter in order to standardize for age. Height, weight, BMI and lnIgE were fit with quadratic models of the form $y = \beta_1 + \beta_2*AGE + \beta_3*AGE^2$, while CRP was fit with a linear model $lnCRP = \beta_1 + \beta_2*AGE$, and weight-for-height as $weight = \beta_1 + \beta_2*height + \beta_3*height^2$. Age terms were highly significant in all models. Model fits were very high for anthropometric measures (height $R^2 = 0.883$, weight $R^2=0.855$, BMI $R^2= 0.548$, WFH $R^2=0.954$) but much weaker for biomarkers which varied significantly around the overall age pattern (lnIgE $R^2 = 0.198$, lnCRP $R^2 = 0.112$). Based on each model, standardized and unstandardized residuals were calculated. Standardized residuals are referred to hereafter with the suffix –SR (e.g. Height-SR), while unstandardized are referred to with the suffix -UR. For the age range includes, there were no significant differences in dependent variables by sex after controlling for age, so variables were not standardized for sex.

Analysis

The basic analyses in study 1 and study 2 were done in PASW Statistics 18.0 for windows (SPSS Inc.), including data transformation, Pearson correlations, t-tests, and ANOVAs. Following common practice, IgE and CRP were log transformed in order to normalize their distributions. The log transformed values are referred to as lnCRP and lnIgE. Before log transformation, CRP was converted into units of mg/ml, instead of the

standard mg/L in order to avoid having negative values after the log transformation. All analyses were done on log-transformed values. T-tests were 2-tailed with equal variance assumed. Parameter estimates were computed using the univariate general linear model procedure.

Analyses in study 3 were done in R 2.9.2 (www.r-project.org). Two types of models were used to estimate the effects of household members on children within the household while simultaneously controlling for the effects of all other household members. The first model is a continuous age model based on the assumption of pooled household effects. The model procedure is a basic version of a model that has been described in detail elsewhere (Chapter II), so we present it only briefly here. The model assumes that the effect (E_i) of household member i is a function of the sex (s) and age (A) of i and can be expressed as a polynomial function of the form:

$$\mathrm{E_i} = (\beta_0 + \beta_{s0}) + (\beta_1 + \beta_{s1})Age_1 + (\beta_2 + \beta_{s2})Age_i^2 + e \qquad (1)$$

For the intercept and each polynomial degree there are two parameters, β_n, the main effect of age, and β_{ns}, the effect of sex on the parameter. The net effect of all family members ($i...j$) on a given household member is the sum of the effects of all household members, E_{total}.

$$E_{total} = (\beta_0 + \beta_{s0})\sum_{i=1}^{j} j + (\beta_1 + \beta_{s1})\sum_{i=1}^{j} Age_1$$

$$+ (\beta_2 + \beta_{s2})\sum_{i=1}^{n} Age_i^2 \ldots + e_{total} \qquad (2)$$

The central insight from equation 2 is that E_{total} is a function of the number of household members of a given sex, the sum of their ages, and the sum of ages squared. The model can be extended to higher polynomial degrees. However, while higher polynomial degrees may describe the age curve more accurately, they are sometimes difficult to interpret in terms of hypothesis testing.

In this study we calculated terms up to the sum of ages cubed ($\sum A^3$). These terms were then entered into a mixed model with random effects correlated by household (the *lme* function in the R *nlme* package). To determine whether a linear or quadratic fit best described the data, and whether there was a significant interaction between sex and age, terms were repeatedly removed and added back in stepwise fashion using the *MASS* package *stepAIC* procedure until the model with the lowest Akaike Information Criterion (AIC) was found (Akaike, 1974).

The second procedure categorizes family members by sex and age groups and for each household counts the number of individuals in each group. It begins with family members under age 49 grouped by five year spans (0-4, 5-9, 10-14, 15-19, etc.) and those over age fifty as a single group (50-69). The initial age groupings were determined based on sample size. For example, there were too few individuals over age fifty to divide these individuals further without singling out individual households.

We wrote a procedure in R to optimize linear models with these age groups. Age group counts were entered into mixed models (*lme* from R package *nlme*) with lnIgE-SR, lnCRP-SR, Height-SR, or Weight-SR as dependent. Since some of the children in the sample come from the same household, all models also had household random intercepts

to control for the correlation between members of the same household and to avoid overestimating the model degrees of freedom for household level variables. Models were fit using maximum likelihood (ML) estimation, instead of the default restricted maximum likelihood (REML) estimation. REML models with different fixed effects cannot be meaningfully compared using AIC, and so could not be used for the model selection procedure. ML models, however, can be compared with AIC. It should be noted that the use of ML models may bias the estimation of random effects to a small degree. However, it does not affect the estimation fixed effects.

Adjacent age groups of the same sex were then summed into a single variable, one at a time (e.g., females 0-4 and 5-9 were combined into females 0-9). The AICs of all models with different combined adjacent groups were then compared to the AIC of the initial model. For each round, the model with the lowest AIC was selected and the procedure was repeated. The procedure continued to combine groups until further combinations did not cause further reductions in AIC. This procedure is essentially equivalent to a backward regression except that variables are combined rather than removed from the model. In this way, all family members continue to be controlled for.

Sample Characteristics

In some studies, individuals with CRP > 10 mg/L are excluded from analysis in order to examine baseline CRP rather than CRP due to acute infection (Pearson *et al.,* 2003; Snodgrass *et al.,* 2003). Following this practice, we excluded one 38 year old female with a CRP of 16 mg/L who was clearly an outlier and likely to be suffering from

an acute infection (the next highest adult CRP was 2.98 mg/L). We considered using similar exclusion criteria for the children under age fifteen. However, the normal distribution of CRP in the children extends much higher than in adults, and it was not clear that the five individuals with CRP > 10 mg/L were outliers (10 mg/L is approximately 2.4 standard deviations above the mean for log-transformed values). We therefore ran analyses both with and without these children. Including the children improved the significance of the findings without changing the direction or magnitude of the effects. We therefore decided to include all children in the analysis. The sample characteristics in Table 5.1 show the final sample after the single exclusion.

Table 5.1. Sample characteristics

		0 to 7		**8 to 15**		**Adults**	
		F (n=31/28)	**M (n=30/27)**	**F (n=36/35)**	**M (n=24/24)**	**F (n=21)**	**M (n=16)**
Age (years)	Mean	5.66	5.97	10.59	10.52	38.46	43.43
	S.D.	1.64	1.61	2.18	1.25	10.59	13.99
Height (cm)	Mean	105.96	106.20	128.69	126.22	147.58	158.28
	S.D.	11.82	10.66	10.51	7.41	4.62	5.41
Weight (kg)	Mean	18.27	18.98	30.51	28.02	54.14	64.45
	S.D.	4.03	4.03	8.31	4.55	8.63	11.80
BMI	Mean	16.13	16.64	18.05	17.46	24.73	25.58
	S.D.	1.03	0.92	2.09	1.08	2.83	3.60
lnIgE (IU/ml)	Mean	6.92	7.14	7.24	7.66	6.48	6.97
	S.D.	1.00	1.00	1.03	0.55	0.82	0.98
IgE (IU/ml)	G. Mean	1,015	1,258	1,392	2,113	653	1,060
lnCRP (mg/ml)	Mean	7.43	7.39	7.06	7.14	7.03	6.91
	S.D.	0.76	0.97	0.78	0.93	0.66	0.59
CRP (mg/L)	G. Mean	1.68	1.62	1.16	1.26	1.13	1.00

Sample sizes (n=x/y) show the total sample for studies 1 and 2 followed by the sample size for study 3, since complete household data was not available on all individuals. Summary statistics are for the complete sample.

Table 5.2. Household composition statistics for the 45 unique families in the sample

	Females				Males			
Ages	**Mean**	**SD**	**Max**	**Sum**	**Mean**	**SD**	**Max**	**Sum**
0 - 4	.89	.88	3	40	.69	.73	3	31
5 - 9	.80	.79	3	36	.82	.86	3	37
10 - 14	.47	.69	2	21	.62	.78	3	28
Total <15	**2.16**	**1.38**	**6**	**97**	**2.13**	**1.44**	**6**	**96**
15 - 19	.36	.61	2	16	.33	.60	2	15
20 - 24	.09	.29	1	4	.07	.25	1	3
25 - 29	.13	.34	1	6	.27	.45	1	12
30 - 34	.24	.43	1	11	.11	.38	2	5
35 - 39	.27	.45	1	12	.16	.37	1	7
Total 15-40	**1.09**	**.63**	**3**	**49**	**.93**	**.69**	**4**	**42**
40 - 44	.18	.39	1	8	.27	.45	1	12
45 - 49	.02	.15	1	1	.04	.21	1	2
50 -70	.11	.38	2	5	.11	.32	1	5
Total 40-70	**.31**	**.51**	**2**	**14**	**.42**	**.50**	**1**	**19**

RESULTS

Study 1: Children's Growth and Immune Function

Objective 1: To examine tradeoffs between branches of immune function

Prediction 1: Inflammation will trade off with humoral responses

Objective 2: To examine tradeoffs between immune function and growth

Prediction 2: Increased investment in immune function will be associated with poorer growth

Age Patterning of IgE and CRP. We have previously described the age profile of Shuar IgE in detail (Chapter IV) so here we do so only only briefly and in order to contrast it

with the age profile for CRP. The age profile of IgE is complex as a result of the dynamics of helminth transmission and the development of a response to helminths (Chapter IV). IgE is very low at birth, and then climbs rapidly to about age six, after which it increases at a much slower rate before reaching a peak around age eleven and then declining (Figure 5.1). In contrast, CRP is highest in the youngest individuals and declines at a more or less linear rate after log transformation (Figure 5.1). The decline in CRP with age is also highly significant ($F_{1,124} = 11.04$, $p < .01$). What the age profiles for CRP and IgE suggest is that early in life innate immunity is the predominant response.

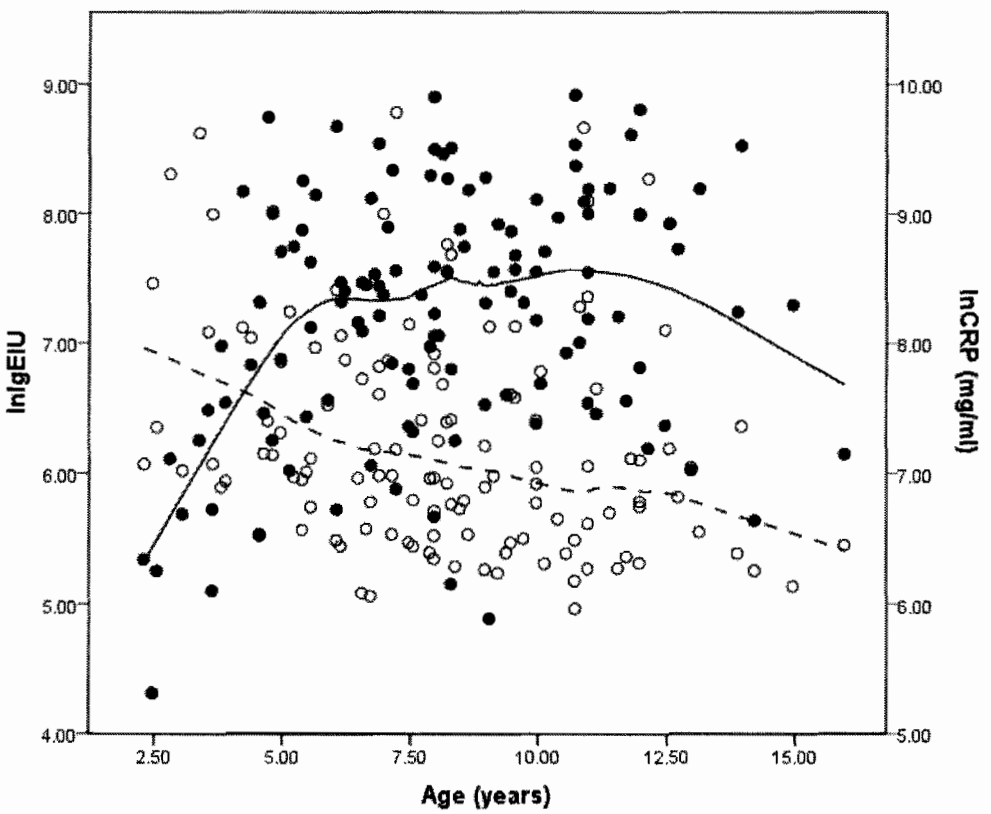

Figure 5.1. Age profiles of lnIgE (solid line, solid circles) and lnCRP (dashed line, open circles). Lines are triweight loess fit lines with a bandwidth of 0.5.

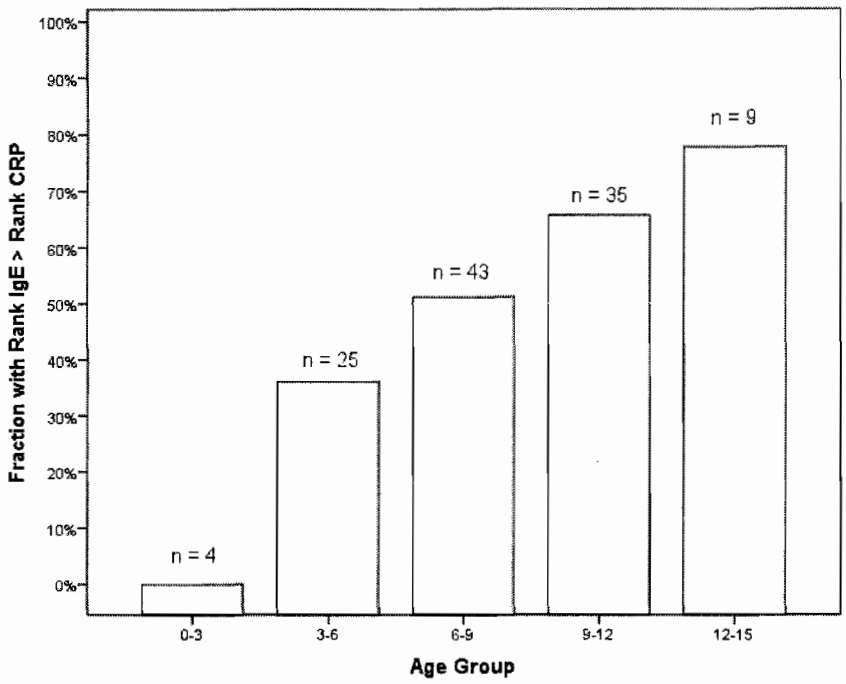

Figure 5.2. Examining the fraction from each age group with rank IgE greater than rank CRP shows a transition between ages 6 and 9 from high ranked CRP to high ranked IgE.

With age humoral defenses are acquired and gradually supplant inflammation as the predominant response (Figure 5.2).

Given the age profiles of IgE and CRP, we would expect them to negatively correlate with one another and this is indeed the case ($r = -.28$, $p < .01$, $df = 126$). However, the correlation persists, even controlling for age (partial correlation controlling for age and age^2, $r = -.21$, $p = .02$, $df = 122$). This suggests that the trade-off between IgE and CRP is not merely a matter of aging, but is a more fundamental feature of the interaction between these two types of response.

Tradeoffs between Immune Function and Growth. We next examined the relationship between growth and immune function. Examining the entire group of children there are no significant correlations between anthropometrics and either lnCRP-SR or lnIgE-SR. Since IgE and CRP are closely linked to age, and since there is a transition in the balance between the two around age seven, we hypothesized that the relationship between IgE, CRP, and growth might also vary with age. We therefore split the sample into two subsamples, age zero to seven, and age eight to fifteen. We chose to divide at age eight because this is close to the approximate age at which the balance between IgE and CRP shifts, and also because this creates two equally sized subsamples. We then ran two types of analyses to examine the relationships between IgE, CRP and growth.

First, we divided the sample based on anthropometric status in height, weight, BMI, and WFH and compared lnCRP and lnIgE in individuals with standardized residuals one standard residual either below or above the mean of zero. For simplicity we refer to these groups as taller/shorter and heavy/lighter, for height and weight, respectively, and as high/low BMI and high/low WFH for BMI and WFH.

For the older children, taller individuals had a geometric mean CRP of 2.0 mg/L, compared to 0.91 mg/L for the shorter individuals ($t=3.45$, $p=.03$, $df=21$) (Figure 5.3). For younger individuals the direction of the effect was reversed: shorter individuals had a geometric mean CRP of 1.6 mg/L vs. 0.87 mg/L in taller individuals ($t=1.72$, $p=.11$, $df=15$). With the two groups entered into an ANOVA together, there is a significant interaction between age group and height status ($F_{1,36}=7.92$, $p < .01$).

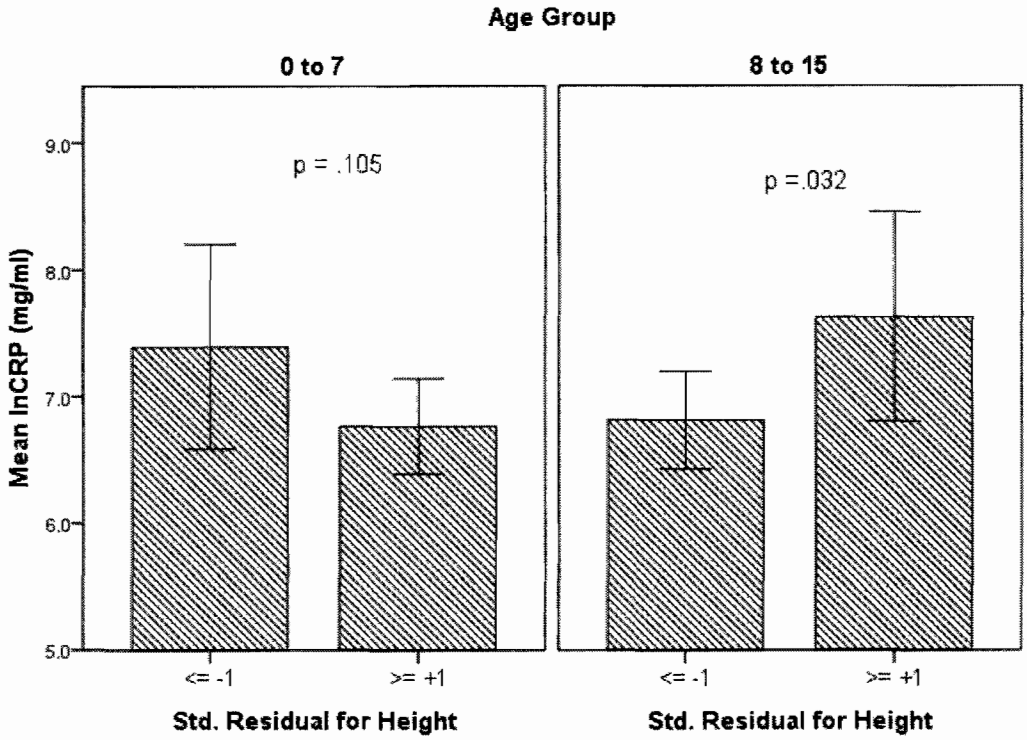

Figure 5.3. Comparison of mean lnCRP in children more than one standard residual above or below the mean for height. Error bars are 95% confidence intervals.

The association with growth is reversed for IgE (Figure 5.4). In the older group shorter individuals have a geometric mean IgE of 2,402 IU/ml, compared to only 804 IU/ml in the taller group ($t=3.45$, $p < .01$, $df=21$). In the younger group IgE is virtually identical in the taller and shorter children (1,630 vs. 1,565 IU/ml, $t=.08$, $p=.93$, $df=15$). As with CRP, we found a significant interaction between age group and height group in predicting IgE levels ($F_{1,36} = 4.18$, $p = .05$). Differences in lnCRP and lnIgE between heavy/lighter, high/low BMI, and high/low WFH were not significant for either age group.

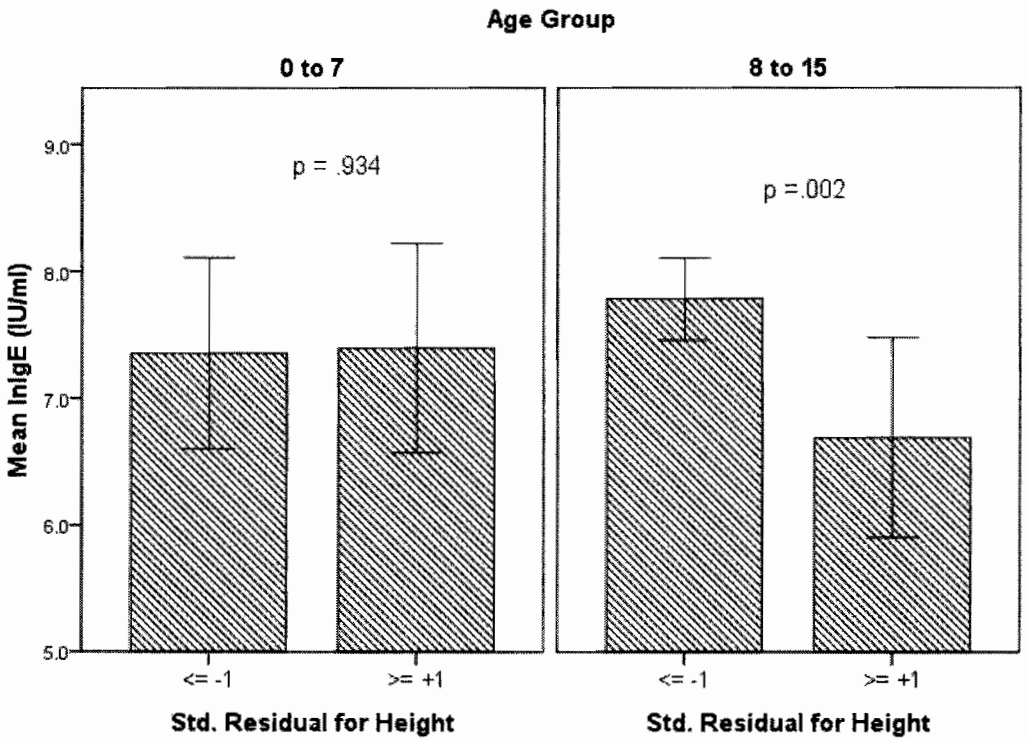

Figure 5.4. Comparison of mean lnIgE in children more than one standard residual above or below the mean for height. Error bars are 95% confidence intervals.

To verify the relationships between height, CRP, and IgE, and to determine whether the effects were dependent on the relative levels of CRP and IgE, we ran linear least squares regression models with height-UR as the dependent variables and either lnIgE or lnCRP as the independent variable. The results for IgE support the conclusion that in 8 to 15 year-olds there is a relationship between Height-UR and lnIgE. For every one unit increase in lnIgE there is a decrease in height of 1.5 cm ($t = -1.96$, $p = .05$). However, there was no significant effect in the 0 to 7 age group ($t = .01$, $p = .99$).

In contrast to IgE, for CRP there was a strong trend in 0 to 7 year-olds. For each one unit increase in lnCRP, height declined by 1.3 cm ($t = -1.82$, $p = .07$) and weight by 0.46 kg ($t = -1.61$, $p = .11$). The parameter for the relationship between lnCRP and height-UR was not significantly different from zero for 8 to 15 year-olds, although it was in the opposite direction compared to the parameter in 0 to 7 year-olds ($\beta = 1.05$, $t = 1.28$, $p = .21$) and the interaction between CRP and age group was significant in an ANOVA with both age groups ($F_{1,121} = 4.64$, $p = .03$).

Discussion for Study 1. Our objectives for the first study were 1) to examine tradeoffs between branches of immune function, and 2) to examine tradeoffs between immune function and growth. We had predicted that 1) inflammation would tradeoff with humoral responses and 2) that increased investment in immune function would be associated with poorer growth.

Our results support our first prediction in two ways. First, the age profile of CRP and IgE suggests an age-dependent transition from a predominantly inflammatory response to a developed humoral response. That this effect is age-dependent does not detract from the life history implications, as many life history trade-offs are by definition age dependent. Second, we find a consistent negative correlation between IgE and CRP. We cannot definitively say that this represents a persistent change in allocation. CRP and IgE may trade-off in the short term in response to new infections, as new infections first trigger inflammatory responses and later humoral responses. However, two factors argue against this interpretation as the sole cause of the negative correlation. First, the

associations between CRP, IgE, and growth argue for persistent effects in these individuals. Second, although IgE fluctuates with factors such as treatment for helminths, high IgE levels persist for a significant length of time in individuals who spent their childhoods in helminth infected areas (Iancovici Kidon *et al.*, 2005).

We also find evidence that immune function trades off with growth, although the picture suggested by the data is somewhat more complex than we had initially predicted. First, IgE is associated with poorer growth, but this effect is much more pronounced later in childhood. In retrospect this finding makes perfect sense: humoral responses take several years to develop and IgE levels do not peak until age eleven. In addition, any physiological factor that has a small but persistent effect on growth will become more apparent later in life as growth insults accumulate. Second, the effect of CRP actually reverses with age. Early in childhood we find a trend in which high CRP is associated with poorer growth, consistent with other published results (McDade *et al.*, 2008). However, we were surprised to find that CRP is associated with better growth later in childhood.

Taking all of these factors into consideration, we suggest the following interpretation: Early pathogenic insults lead to generic inflammatory responses, as evidenced by high CRP. CRP is therefore associated with early pathogenic insults and corresponding reductions in growth. However, these early insults trigger the development of specific defenses and affect the T_H1/T_H2 balance. We therefore predict that children who have high CRP in early childhood will actual grow up to have lower CRP and higher IgE later in childhood, due to early shifting of this balance. With more

energy shifted into specific, humoral responses (IgE), less is directed towards growth. Thus, children with high IgE and low CRP later in life should have poorer growth. Finally, children who do not tune their immune systems early on must rely on generic responses later in life. High CRP and low IgE later in life are therefore indicative of an early childhood free of heavy pathogenic burden. We caution that this interpretation is somewhat speculative. It is consistent with the findings in this study, but cannot be fully supported without longitudinal data to back up the cross-sectional data presented here. However, this interpretation actually leads to specific predictions about the relationship between height and trade-offs between branches of immune function in adults. Study 2 examines these trade-offs.

Study 2: Adult Anthropometrics and Immune Function

Objective: To examine the relationship between growth, CRP, and IgE in Shuar adults.
Prediction: If immune function allocations are persistent throughout the life span, then adult height should be correlated with levels of IgE and CRP. Specifically: 1) Taller adults should rely more on generic immune responses like inflammation, and so have higher CRP, and 2) Shorter adults should have immune system more finely tuned to local environments, as evidenced by higher IgE.

To test these predictions, we used the available sample of adults over age eighteen (21 females, 16 males) from the same village as the children in study one. Scatterplots of

IgE and CRP versus anthropometrics suggest that IgE is associated with shorter stature and CRP with taller (Figure 5.5). We used least squares models to estimate parameters for the relationship between IgE and CRP and anthropometric variables (Table 5.3). All models controlled for sex and age. We find highly significant negative partial correlations between IgE and adult anthropometrics. In fact, IgE accounts for 26% of the variance in height, 25% of the variance in weight, and 20% of the variance in BMI. For every one unit increase in lnIgE, adult height decreases by 2.8 cm ($t = -3.29$, $p < .01$), weight by 5.7 kg $t = -3.24$, $p < .01$), and BMI by 1.6 kg/cm^2 ($t = -2.80$, $p < .01$).

CRP is positively correlated with all three variables, though to a less significant degree. CRP accounts for only 7% of the variance in height, 15% of the variance in weight, and 16% of the variance in BMI. Each one unit increase in CRP is associated with an increase of 2.0 cm in height ($t = 1.56$, $p=.13$), an increase of 6.4 kg in weight ($t = 2.42$, $p=.02$) and an increase of 2.0 kg/cm^2 in BMI ($t = 2.48$, $p=.02$).

Table 5.3. Least squares regression parameter estimates for the effect of biomarkers on adult anthropometrics

Ind.	Dep.	β	SE	t	p	Age (p)	Sex (p)	Partial η^2
lnCRP	Height (cm)	2.03	1.30	1.56	.128	.216	.000	.068
	Weight (kg)	6.20	2.56	2.42	.021	.581	.001	.150
	BMI	2.00	.81	2.48	.019	.907	.289	.157
lnIgE	Height (cm)	-2.81	.85	-3.29	.002	.259	.000	.256
	Weight (kg)	-5.67	1.75	-3.24	.003	.578	.000	.251
	BMI	-1.59	.57	-2.80	.009	.869	.081	.199

Models include the independent variable, intercept, age, and sex. For reference, the p-values for the age and sex control variables are shown.

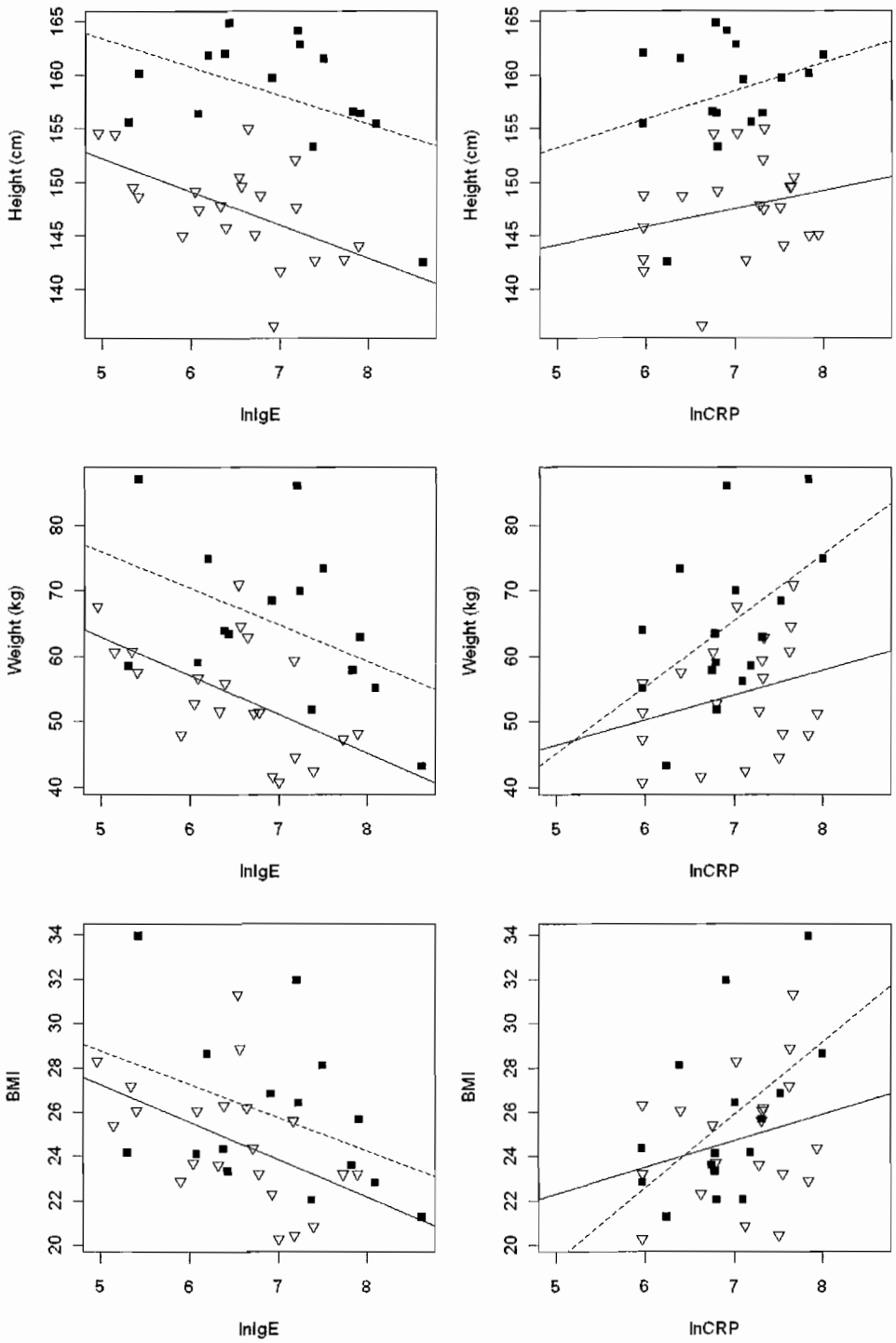

Figure 5.5. Relationships between biomarkers and anthropometrics in Shuar adults. Males are indicated with filled circles and dashed lines, females with open triangles and solid lines.

Discussion for Study 2. In Study 2 we examined the relationship between anthropometrics and biomarkers in a small sample of Shuar adults. Consistent with the hypothesis that early developmental events cause persistent changes in immune function, we find strong negative correlations between biomarkers and anthropometrics in adults. This suggests that a history of poor growth resulting in smaller adult size is associated with continued investment into immune function in adults.

From a Western perspective, the fact that IgE accounts for 25% of the variance in height may seem incredible, given the dramatic between individual variation in height in places like the United States. However, it is important to remember that North Americans come from a wide variety of backgrounds with different genetic dispositions, family histories, and so on. The Shuar adults in this study are from a single village composed primarily of three or four extended families. In fact, based on genealogies we collected in the village we calculate that the mean coefficient of relatedness between the adults in this study is .026 (SD +/- 0.10), approximately equivalent to the relatedness of second cousins. Thus, all of the individuals in this study not only the same ethnic background but are also closely related to one another. It is therefore likely that they share similar genetic propensities and potentials for growth. As a consequence we would expect a greater percentage of the variation in anthropometrics in this population to be due to environmental and developmental factors, while the heritable variance should be low.

Study 3: Effect of Household Members on Growth and Immune Function

Objective: To examine the effect of household members on growth, IgE, and CRP.

H1: Cooperative Breeding/Phenotypic correlation. Predictions: Additional adult household members will be associated with *higher* growth measures and *higher* investment into costly immune responses (IgE), due to an increase in available energy. Although growth and immune response trade-off, when more energy is available it will be using to increase both branches of the trade-off.

H2: Quantity-Quality Hypothesis. Predictions: Since parental investment is limited, more dependents should mean less investment for each. Controlling for household producers, an increased number of household dependents will be associated with *lower* investment into costly immune responses (IgE) and *poorer* growth, due to lower overall energy

H3: Disease Transmission. Predictions: More children in the household will mean greater opportunity for exposure to communicable pathogens. Controlling for total energy, the number of children in the household will be correlated with *increased* allocation of resources towards immune function (IgE) and *decreased* allocation toward growth.

In study 3 we test a number of hypotheses derived from life-history theory and relating to the relative allocations of resources between competing demands. The hypotheses for this study all relate to the relative ways in which we expect household members to affect growth and the immune responses indicated by levels of CRP and IgE. The predictions can be generally summarized as follows: increased energy should lead to increases in both costly immune defenses and growth, while increased exposure to pathogens should shift the relative allocation of energy between immune function and growth. For the most part, this general proposal leads to clear predictions about the effects family members should have on growth and immune function. However, some aspects are less clear. In particular, hypothesis 2 and hypothesis 3 predict opposite effects for increasing numbers of children in the household on immune function, since more children are expected to both decrease energy available for immune function and increase demand for immune function by increasing pathogen exposure.

Modeling Strategy. We used two types of mixed effect models to examine the effect of household members on biomarkers and anthropometrics, while controlling for correlations between members of the same household with a household level random effect. The first is a continuous model that includes terms for the number of household members as well as sums of household member's ages. The model is derived as the sum of the effects of each individual household member. As a consequence, the results from this model can be interpreted in two ways. First, the parameter estimates describe the effect of an individual household member on a particular dependent variable (height, for

example) as a function of age. Second, the terms can be taken literally: the first term is the number of household members, and the second term is the cumulative age of the household.

The second type of model is a more traditional categorical model that groups household members by age and examines the effect of each category on the dependent variable, controlling for household members in other categories. However, unlike analyses that have been done in the past, we allow the categories to be determined dynamically through AIC minimization. The categorical model begins with household members under the age of fifty grouped into five year age categories, and those 50-70 in a single category. It then combines age categories one at a time, comparing the fit of the model with the combined categories to the original model. This process continues until the AIC reaches a minimum. In order to control for the effects of all household members, categories are never removed from the model, only summed together.

For both types of model we examined the overall effect of age categories and then tested for significant interactions with sex. For the continuous model a few small effects were found, but in general sex differences were not apparent. We also found no consistent sex differences using the categorical model—in part this appeared to be due to significant covariance between males and females in a given age category—for example most families with a female over age fifty also had a male over age fifty. For this reason we report only the overall age category effects for the continuous model.

Model Fit and Random Effects. Before examining the fixed effects in these models, we first examined the random variance components (Table 5.4). The variance components allow us to determine, 1) how much of the variance between individuals is attributable to household differences, and 2) how much of the household level variance was explained by each model. For height, weight, and IgE household accounts large portions of the variance. In children 0 to 7, 16% of the variance in height and weight is explained by household, while household accounts for 15% of the variance in IgE. For 8 to 15 year-olds the variance in height and weight due to household increases to 42-52%, while the variance in IgE due to household increases to 47%. Overall, 22% of the variance in height, 30% of the variance in weight, and 31% of the variance in IgE is due to household. In contrast, a 24% of the variance in CRP is due to household at younger ages, but essentially none of the variance in 8 to 15 year-olds, and only 3% overall.

The models do a very good job of explaining the household variance in height, weight, and IgE. In general the categorical models explain a greater degree of the variance and fit the data better than the continuous models, although this is not the case for CRP in children 8 to 15 and overall. In children 0 to 7 the categorical models explain 100% of the household variance in height, IgE, and CRP, and 48% of the variance in weight. In juveniles 8 to 15, the categorical models explain 76% of the household variance in height, 46% of the variance in weight, and 35% of the variance in IgE. The continues model for CRP in the 8 to 15 year-old group explains 71% of the small amount of variance due to household.

Table 5.4. Variance due to household in the null model and each explanatory model

		0 to 7			8 to 15			Overall		
		% σ^2 HH	% Δ σ^2 HH	AIC	% σ^2 HH	% Δ σ^2 HH	AIC	% σ^2 HH	% Δ σ^2 HH	AIC
Height-SR	Null	16	-	154.64	42	-	173.26	22	-	324.51
	Cont.	1	95	151.44	36	24	171.01	14	42	319.94
	Cat	< 1	100	150.96	15	76	161.24	5	80	309.13
Weight-SR	Null	16	-	113.28	52	-	188.72	30	-	319.18
	Cont.	16	0	113.28	44	30	185.73	24	29	313.68
	Cat	10	48	110.57	38	46	181.39	19	47	306.41
lnIgE-SR	Null	15	-	162.35	47	-	171.57	31	-	323.73
	Cont.	7	59	162.08	38	29	171.06	26	25	321.33
	Cat	< 1	100	160.22	35	35	170.50	24	30	324.08
lnCRP-SR	Null	24	-	168.94	< 1	-	176.65	3	-	340.24
	Cont.	24	0	168.94	< 1	71	173.97	3	10	338.63
	Cat	< 1	100	166.57	< 1	55	174.22	2	58	338.82

% σ^2 HH = random variance attributable to household, rather than individual variation.
% Δ σ^2 HH = percent reduction in household attributable variance compared to the null model

Fixed Effects. We first modeled the effects of family members on Height-SR (Figure 5.6; Tables 5.5 and 5.6). Using the continuous model (Table 5.5), we find that additional family members have negative effects at age zero. Each additional family member decreases Height-SR by 0.22 SR (~1.13 cm) ($t = -2.52$, $p = .01$). However, the effect becomes significantly more positive the older the family member is (or the older the cumulative family age is), with each year of age making the effect 0.10 SR more positive ($t = 3.31$, $p < .01$). Female family members also have effects that are somewhat more positive. As a consequence, males over age 22 and females over age 10 have net positive effects on height.

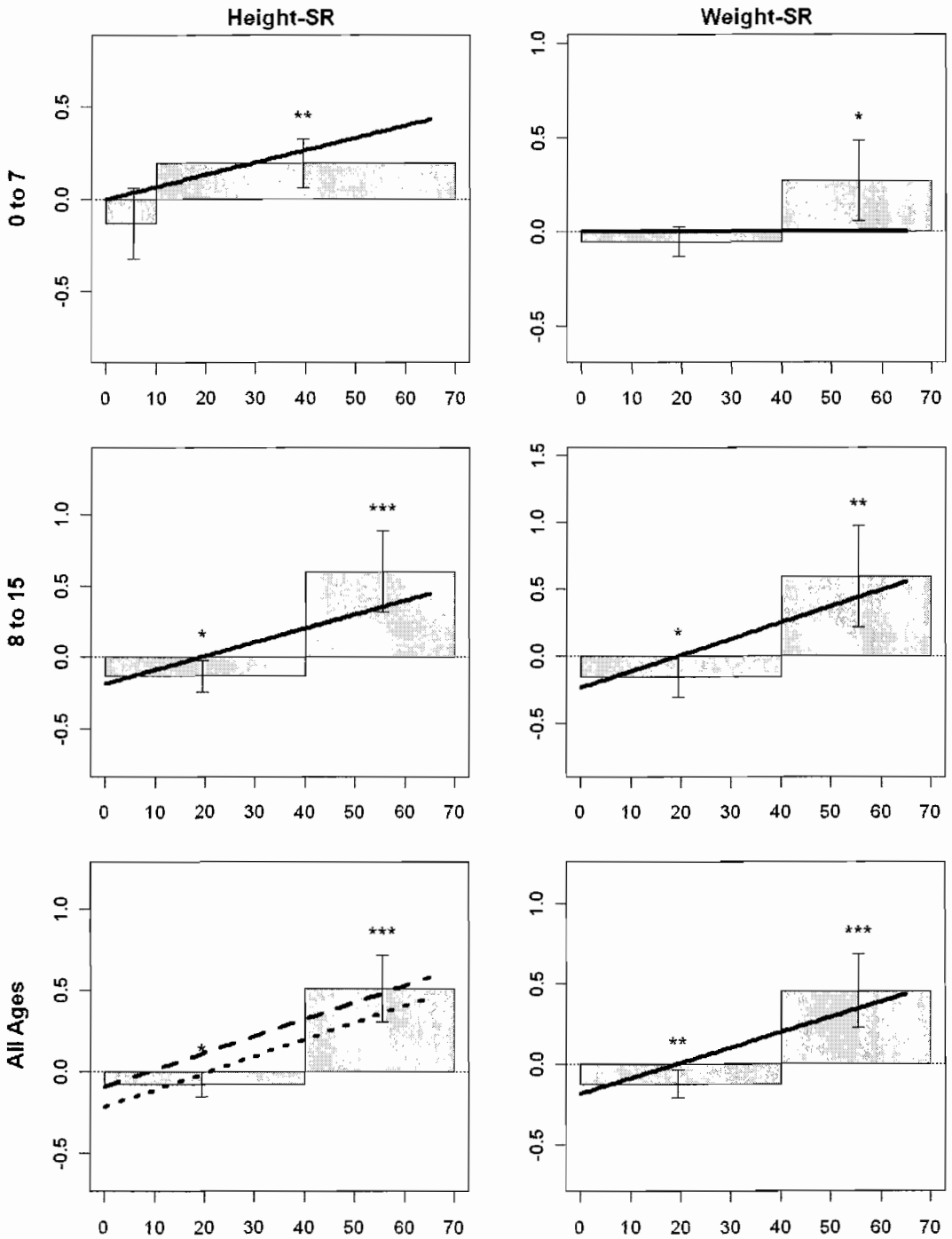

Figure 5.6. Effect of household members on standardized residuals for height, and weight. Lines show the significant effects from the continuous mixed model for males (short dashes), females (long dashes), and overall with no sex effect (solid line). Bars show the parameter coefficients from the categorical mixed model. Error bars are 95% confidence intervals. Symbols indicate parameter significance in a 2-tailed t-test: *** $p \leq .001$, ** $p \leq .01$, * $p \leq .05$, t $p \leq .10$

Table 5.5. Results for the continuous effects mixed model regression on Height-SR

Ages	Parameter	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	(Intercept)	-.738	.338	35	-2.182	.036*	.007	.719
	∑ Ages	.007	.003	35	2.447	.020*		
8 to 15	(Intercept)	.038	.520	30	.072	.943	.338	.591
	HH Members	-.186	.089	27	-2.087	.046*		
	∑ Ages	.010	.004	27	2.495	.019*		
All Ages	(Intercept)	-.182	.318	69	-.572	.569	.118	.713
	HH Members	-.216	.086	69	-2.522	.014*		
	∑ Ages	.010	.003	69	3.308	.001**		
	Females	.123	.080	69	1.534	.130		

Note: For reference, one SR unit in height is ~5.19 cm

Table 5.6. Results for the categorical mixed model regression on Height-SR

Ages	Age Group	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	Intercept	-.231	.374	34	-.617	.541	.000	.694
	0 - 9	-.129	.097	34	-1.327	.193		
	10 - 69	.195	.067	34	2.919	.006**		
8 to 15	Intercept	.367	.432	30	.850	.402	.107	.631
	0 - 39	-.135	.056	27	-2.399	.024*		
	40 - 69	.599	.142	27	4.208	.000***		
All Ages	Intercept	.107	.286	70	.373	.710	.040	.717
	0 - 39	-.078	.040	70	-1.952	.055 t		
	40 - 69	.510	.105	70	4.848	.000***		

Note: For reference, one SR unit in height is ~5.19 cm

Using the categorical modeling procedure family members end up grouped into two age categories, < 40 and ≥ 40. Family members under age 40 have a net negative effect on height, although the effect is small (~0.41 cm/person, $t = -1.95$, $p = .06$). In contrast the effect of family members over 40 is large and highly significant, with each family member increasing height by ~2.65 cm ($t = 4.85$, $p<.01$).

We next examined the effects of family members separately for 0 to 7 year olds and 8 to 15 year olds. The effect of family members on Height-SR varies slightly with the age of the child whose height is in question. In the continuous model negative effects of more family members are not apparent in children age 0 to 7, while they are in those age 8 to 15 (Table 5.5). In the categorical model, the effects of family members on juveniles8 to 15 mirror the overall results for all ages, with those < 40 having negative effects and those ≥ 40 having positive effects (Table 5.6). In contrast, in the 0 to 7 year-olds individuals ≥ 10 have positive effects on height, equivalent to ~1.0 cm per family member ($t = 2.92$, $p < .01$).

The results for weight closely mirror the results for height (Figure 5.6 Table 5.7, and Table 5.8). In the continuous model (Table 5.7) household members have a negative effect on weight at age zero, with each decreasing weight by ~0.56 kg ($t = -2.77$, $p < .01$). However, the effect becomes increasingly positive with age, such that family members over 18 have positive effects on weight ($t = 3.12$, $p < .01$). Examined with the categorical model (Table 5.8), household members < 40 have a negative effect on weight, decreasing weight by ~0.37 kg each ($t = -2.74$, $p < .01$). Household members ≥ 40 have positive effects equivalent to 1.40 kg each ($t = 3.88$, $p < .01$).

We again divided the analysis into two age ranges. As with height, effects were greater in 8 to 15 year-olds than they were in 0 to 7 year-olds, regardless of the modeling procedure used (Tables 5.7 and 5.8). In the categorical models age groups were combined into two groups, < 40 and ≥ 40, with those < 40 having negative effects in both age groups and those ≥ 40 having positive effects. Using the continuous model the age

Table 5.7. Results for the continuous effects mixed model regression on Weight-SR

Ages	Parameter	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	(Intercept)	.048	.089	37	.538	.594	.064	.325
8 to 15	(Intercept)	.137	.612	30	.224	.824	.537	.695
	HH Members	-.239	.104	27	-2.291	.030*		
	∑ Ages	.012	.005	27	2.666	.013*		
All Ages	(Intercept)	.159	.334	70	.476	.635	.200	.630
	HH Members	-.182	.066	70	-2.768	.007**		
	∑ Ages	.010	.003	70	3.119	.003**		

For reference, one SR unit in weight is ~3.06 kg

Table 5.8. Results for the categorical mixed model regression on Weight-SR

Ages	Age Group	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	Intercept	.220	.267	34	.824	.416	.033	.310
	0 - 39	-.052	.039	34	-1.326	.194		
	40 - 69	.272	.108	34	2.531	.016*		
8 to 15	Intercept	.545	.573	30	.952	.349	.417	.694
	0 - 39	-.160	.075	27	-2.127	.043*		
	40 - 69	.591	.189	27	3.127	.004**		
All Ages	Intercept	.458	.313	70	1.463	.148	.149	.617
	0 - 39	-.122	.044	70	-2.737	.008**		
	40 - 69	.456	.117	70	3.884	<.001***		

For reference, one SR unit in weight is ~3.06 kg

pattern was not significant in 0 to 7 year-olds, but was highly significant in juveniles 8 to 15.

We next examined the effects of household members on lnIgE-SR (Figure 5.7; Tables 5.9 and 5.10). The pattern of effects for lnIgE was more complex than the pattern for either height or weight. In the continuous models quadratic and cubic terms were required to adequately describe the age pattern (Table 5.9). Overall, the continuous

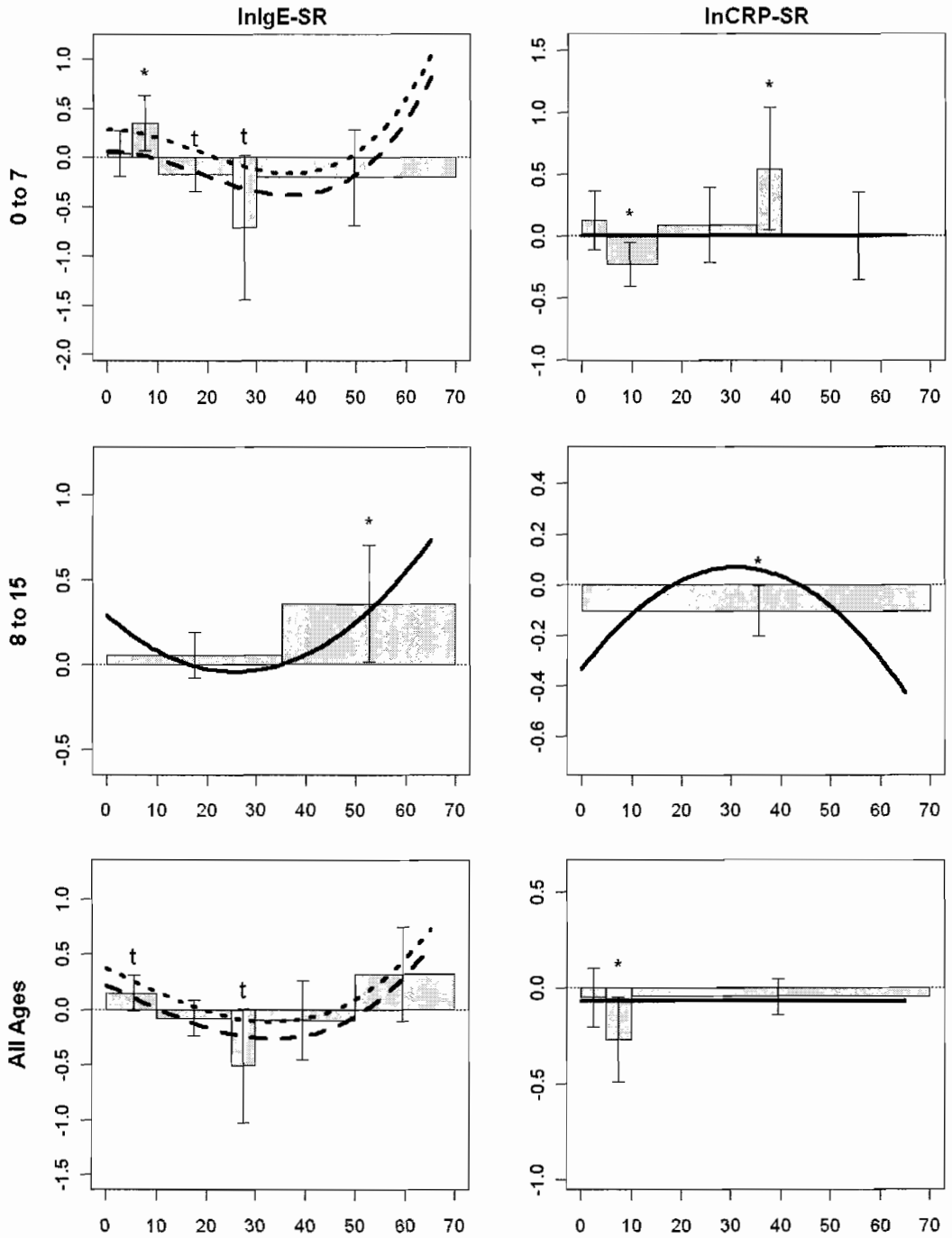

Figure 5.7. Effect of household members on standardized residuals for lnIgE, and lnCRP. Lines show the significant effects from the continuous mixed model for males (short dashes), females (long dashes), and overall with no sex effect (solid line). Bars show the parameter coefficients from the categorical mixed model. Error bars are 95% confidence intervals. Symbols indicate parameter significance in a 2-tailed t-test: *** $p \leq .001$, ** $p \leq .01$, * $p \leq .05$, t $p \leq .10$.

Table 5.9. Results for the continuous effects mixed model regression on lnIgE-SR

Ages	Age Group	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	(Intercept)	-.038	.423	32	-.090	.929	.058	.730
	HH Members	.285	.122	32	2.339	.026*		
	$\sum$ Ages^2	-.001	.001	32	-1.946	.060t		
	$\sum$ Ages^3	.000	.000	32	2.070	.047*		
	Females	-.221	.113	32	-1.953	.060t		
8 to 15	(Intercept)	-.964	.525	30	-1.837	.076t	.349	.559
	HH Members	.289	.155	26	1.866	.073t		
	$\sum$ Ages	-.026	.017	26	-1.513	.142		
	$\sum$ Ages^2	.001	.000	26	1.696	.102		
All Ages	(Intercept)	-.475	.347	68	-1.367	.176	.225	.639
	HH Members	.375	.131	68	2.871	.005**		
	$\sum$ Ages	-.022	.009	68	-2.471	.016*		
	$\sum$ Ages^3	.000	.000	68	2.568	.012*		
	Females	-.154	.091	68	-1.695	.095t		

For reference, one SR unit in lnIgE is ~0.86 ln IU/ml

Table 5.10. Results for the categorical mixed model regression on lnIgE-SR

Ages	Age Group	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	Intercept	.287	.615	31	.466	.644	.000	.735
	0 - 4	.040	.119	31	.339	.737		
	5 - 9	.351	.145	31	2.419	.022*		
	10 - 24	-.171	.091	31	-1.873	.070t		
	25 - 29	-.710	.380	31	-1.866	.072t		
	30 - 69	-.203	.252	31	-.807	.426		
8 to 15	Intercept	-.976	.506	30	-1.927	.064t	.319	.596
	0 - 34	.056	.067	27	.836	.411		
	35 - 69	.361	.173	27	2.080	.047*		
All Ages	Intercept	-.118	.450	68	-.262	.794	.211	.652
	0 - 9	.150	.081	68	1.853	.068t		
	10 - 24	-.078	.083	68	-.942	.349		
	25 - 29	-.507	.267	68	-1.901	.062t		
	30 - 49	-.096	.183	68	-.527	.600		
	50 - 69	.321	.215	43	1.491	.143		

For reference, one SR unit in lnIgE is ~0.86 ln IU/ml

model suggests that household members have a positive effect on IgE at age zero, but that this effect declines with age and becomes negative for females between the ages of 10 and 50 and males between 20 and 45. Adults over age 45-50 have positive effects on IgE. Throughout the lifespan, male household members have greater effects than females.

Although the continuous model provides the best fit for IgE (Table 5.4), the overall pattern is mirrored in the categorical model (Table 5.10). Zero to nine year-olds have a positive effect equivalent to an increase in lnIgE of 0.13 ln(IU)/ml ($t = 1.85$, $p = .07$). Adults 10 to 49 are associated with lowered lnIgE-SR, with the greatest effect from those 25 - 29 ($t = -1.90$, $p=.06$). Household members ≥ 50 trend towards having a positive effect on IgE ($t = 1.49$, $p=.14$). Although these categorical results are non-significant they support they conclusions from the continuous model.

We next examined the effect of household members on lnIgE in children separated by age into 0 to 7 and 8 to 15 year-olds. Although the continuous models for both age groups show similar parabolic shapes, examined with the categorical models different individuals appear to be have primary effects. In the younger age group juveniles 5-9 have significant positive effects on IgE ($t = 2.42$, $p = .02$), while those 10-29 have negative effects, with the greatest negative effects in those 25-29 ($t = -1.87$, $p = .07$). Adults over age thirty have non-significant negative effects on IgE.

In the 8 to 15 year-olds, 0 to 24 year-olds have no significant effect on IgE. Adults over 35 have a significant positive effects on IgE, equivalent to an increase of 0.31 ln(IU)/ml per person ($t = 2.08$, $p = .05$). The overall differences between the two

age groups are intriguing, because they suggests different types of effects from different household members at different points during development. We conclude that children and young adults have primary effects on IgE early in life while, older adults have primary effects later.

Finally, we examined the effects of family members on CRP (Tables 5.11 and 5.12), keeping in mind the fact that household membership explains very little of the variance in CRP. For CRP the categorical model had the best AIC for the younger children, and the continuous model had the best fit in the older children. Overall, the continuous model suggests that household members have a negative effect on CRP ($t = 1.94$, $p = .06$) while in the categorical model only 5-9 year-olds have a significant negative effect ($t = -2.43$, $p = .02$). In the younger group household members age 5 to 14 had significant negative effects on CRP ($t = -2.52$, $p = .02$), while individuals 35-39 had significant positive effects ($t = 2.11$, $p = .04$). In 8 to 15 year-olds the categorical model suggests that all household members have negative effects on CRP ($t = -2.11$, $p=.04$) but did not distinguish by age range. In contrast, the continuous model for CRP suggests a parabolic shape mirroring the shape seen for IgE, but in reverse. Young household members have net negative effects on CRP, equivalent to 0.28 ln(mg)/ml. This negative effect gradually becomes a positive effect around age 18, but declines again, such that household members > 45 have negative effects.

Discussion for Study 3. In study 3 we examined the effect of household members on biomarkers and anthropometrics in order to evaluate four hypotheses. The first of these

Table 5.11. Results for the continuous effects mixed model regression on lnCRP-SR

Ages	Age Group	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	(Intercept)	.049	.149	37	.331	.743	.252	.794
8 to 15	(Intercept)	.953	.438	30	2.177	.037*	.000	.871
	HH Members	-.337	.127	26	-2.652	.013*		
	$\sum$ Ages	.026	.014	26	1.885	.071t		
	$\sum$ Ages^2	.000	.000	26	-1.735	.095t		
All Ages	(Intercept)	.616	.317	71	1.942	.056t	.031	.958
	HH Members	-.072	.038	71	-1.897	.062t		

For reference, one SR unit in lnCRP is ~0.84 ln mg/ml

Table 5.12. Results for the categorical mixed model regression on lnCRP-SR

Ages	Age Group	β	SE	df	t	p	σ^2 HH	σ^2 Res.
0 to 7	Intercept	.129	.422	31	.307	.761	.000	.822
	0-4	.125	.123	31	1.014	.319		
	5 - 14	-.232	.092	31	-2.524	.017*		
	15 - 34	.087	.156	31	.558	.581		
	35 - 39	.541	.256	31	2.113	.043*		
	40 - 69	-.001	.184	31	-.008	.994		
8 to 15	Intercept	.934	.436	30	2.142	.040*	.000	.935
	0 - 69	-.105	.050	28	-2.110	.044*		
All Ages	Intercept	.837	.327	69	2.560	.013*	.014	.942
	0-4	-.053	.078	69	-.682	.497		
	5 - 9	-.272	.112	69	-2.427	.018*		
	10 - 69	-.048	.047	69	-1.018	.312		

For reference, one SR unit in lnCRP is ~0.84 ln mg/ml

predicts phenotypic correlation between growth and immune defense when total energy is not controlled for. We had predicted that an increased number of household producers would be associated with increases in both growth and IgE. We find that this is the case with producers defined as adults over age forty. Older adults have positive effects on

Consistent with the hypothesis that older adults provide resources which lead to correlated increases in both IgE and growth, we examined the trade-off between these factors controlling for older adults (Table 5.13). Adding this control significantly increases the trade-off between height and IgE, and also significantly improves model fit.

An alternate hypothesis for why older adults might increase both growth and immune function is that older adults might both provide resources and increase disease transmission to children in the household. This might be the case if older adults suffer from increased morbidity compared to younger adults. However, arguing against this hypothesis is the fact that the effect of older adults on IgE is significant only in 8 to 15 year-olds, whereas younger family members have significant effects in 0 to 7 year-olds.

Table 5.13. Trade-off between Height-SR and lnIgE-SR in 8 to 15 year olds, controlling for older adults in the household

	Parameter	**β**	**SE**	**df**	**t**	**p**
Model 1	(Intercept)	-.169	.164	30	-1.031	.311
	lnIgE-SR	-.231	.130	28	-1.780	.086t
Model 2	(Intercept)	-.659	.181	30	-3.633	.001**
	lnIgE-SR	-.279	.118	27	-2.368	.025*
	Adults 40-70	.594	.150	27	3.954	.001***

	AIC	**BIC**	**logLik**	**σ^2 Household**	**σ^2 Residual**
Model 1	172.15	180.52	-82.07	.476	.556
Model 2	161.16	171.63	-75.58	.190	.566

This suggests that older adults are not causing high IgE to develop earlier, as would be predicted if transmission were greater.

A positive role for older family members is also consistent with data from other foraging societies, suggesting that older individuals supplement the production of juveniles and reproductive age women (Kaplan *et al.*, 2000). It remains an open question whether males or females are more important, with many studies focusing on the effects of older females (Gibson & Mace, 2005; Hawkes *et al.*, 1997; Mace & Sear, 2005; Sear *et al.*, 2000; Sear *et al.*, 2002). In this study males had greater effects on IgE, although this was not specific to older males. However, this effect is unlikely to be due to energy. Males in most populations have consistently higher IgE (Chapter IV). It may be that males are more susceptible to helminth infections, giving them higher IgE and also making them more effective disease vectors. In contrast, females in this study had greater positive effects on height. Again, this could be due to energy production or differences in disease susceptibility and transmission. Unfortunately, given the sample characteristics we were not able to further separate effects by sex, so we cannot conclusively evaluate their relative importance.

The effects of younger adults, 15 to 39, were somewhat more difficult to interpret. These individuals were associated with small increases in height and decreases in IgE in younger children, but with lower height and weight in older children. Our personal experiences in the field tell us that these individuals are working hard to provide for their families. However, it may be that the effects of additional alloparents in this age range come primarily via decreases in early disease transmission, perhaps through improved

hygiene or increasing carrying of infants. It may also be that any additional resources produced by individuals of reproductive age go into producing more offspring, diluting most of the additional benefits from having these individuals in the household.

Our second hypotheses predicted that parents would face a quantity-quality trade-off, with additional dependents in the household leading to decreases in both growth and IgE due to competition for resources. However, we had also predicted that this would be confounded by increased disease transmission among large families, with children in households with many dependents having poorer growth, but higher relative IgE. In this study we find that additional children are indeed associated with higher IgE and poorer growth. However, these two effects are separated temporally. The positive effects on IgE occur primarily in younger children, while the negative effects on growth are most apparent in older children. The results are consistent with more children being associated with increased disease transmission, causing earlier development of high IgE and redirection of resources from growth toward immune function. However, competition for resources may also play a role in this process. In fact, the negative association between children and both height and weight in 8 to 15 year olds, and the lack of a positive association with IgE may mean that those in large households are sacrificing growth to simply maintain the same IgE levels. However, these findings illustrate the difficulty of detecting quantity-quality tradeoffs. The only criteria by which the relative evolutionary value of greater stature versus higher defenses against parasites can be judged is in the effects of each on fitness itself.

A Unified Model for the Effects of Household Members

We developed a working model to position the various effects found in this study into a unified framework (Figure 5.8). In the model household members have two basic pathways through which they can affect trade-offs: 1) by affecting energy availability and 2) by affecting disease transmission. Our data leads us to expect that older adults contribute by providing extra energy which is directed exclusively towards existing descendents. Reproductive age adults also contribute energy, but they also produce additional offspring, negating their excess production capacities. Children, in turn, are

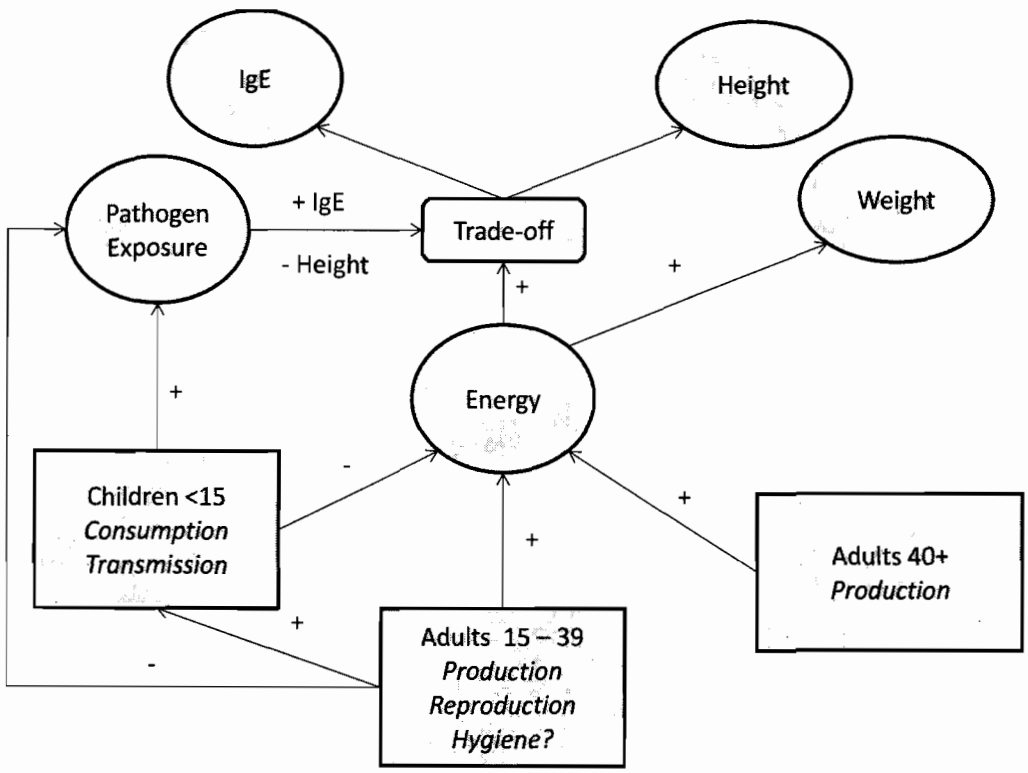

Figure 5.8. Hypothesized relationships between family members and allocations between growth and IgE

net consumers, reducing the overall pool of energy available. The overall pool of energy contributes to all branches of the trade-off, increasing IgE, height, and weight. Pathogen exposure is affected primarily by children and by reproductive age adults. We hypothesize that children increase exposure to pathogens (in this case helminths) by acting as vectors and by increasing density within the household. Reproductive age adults can counter this tendency through hygiene and by carrying children, which limits the transmission of soil-borne helminths. Pathogen exposure acts on the allocation of energy between growth and immune function, with height being much more susceptible to trade-offs than weight.

General Discussion

We began by examining trade-offs between growth, IgE and CRP in Shuar children. In older children IgE was associated with shorter stature, a pattern that was also highly significant among Shuar adults. From a public health perspective, this finding is of critical importance. Intestinal helminths infect around a billion people worldwide and a disproportionate number of these individuals belonging to indigenous populations. Yet the health effects of helminths are often overlooked or underappreciated (Hotez *et al.,* 2008; Hurtado *et al.*, 2004; Hurtado *et al.*, 2008). The association between stature and IgE argues for lasting health consequences from helminth infections. Native South Americans experience a disproportionate degree of stunting compared to other native groups (Blackwell *et al.,* 2009; Victora, 1992). At the same time, they experience high a prevalence of helminth infection and have some of the highest known levels of IgE

(Chapter IV). Stunting among South Americans has traditionally been blamed on nutritional factors, yet our results argue that helminth infections are likely to be an important determinant as well.

In younger children we found that higher CRP was associated with shorter stature, consistent with other reports (McDade *et al.*, 2008). But in older children, adolescents, and adults, CRP was associated with greater stature. From the standpoint of life history theory, this pattern makes sense. IgE is likely to be a costlier form of immune response than is inflammation, and we have provided limited evidence for a trade-off between IgE and CRP. However, this finding may seem surprising to a Western audience. CRP in Western population is generally associated with "unhealthy" outcomes such as increased cardiovascular risk, and has been shown to negatively correlate with things such as fat free mass (Lassek & Gaulin, 2009). However, among other foragers, CRP is not associated with cardiovascular disease (Gurven *et al.*, 2009). In both cases CRP likely represents a generic response to pathogens. It is the alternative to CRP that likely varies between Western and developing societies. For the Shuar, the alternative is an even costlier type of defense. For North Americans the alternative is likely no defense at all, given our highly sanitized environment.

We have interpreted the finding that IgE is associated with poorer growth as evidence that IgE is costly to produce and maintain. An important caveat on this interpretation is that we cannot completely separate the costs imposed by parasite load and the costs entailed in defending against parasites. It may be that production of humoral responses is not itself costly, but that the cost comes from the parasite that

causes the rise in IgE. However, a number of studies have shown that IgE is associated with improved resistance to helminths, and frequently with lower pathogen loads (Chapter IV). We therefore suspect that although individuals with high IgE are likely to have had earlier exposure to pathogens, or perhaps higher loads at some time in the past, they are unlikely to have consistently higher pathogen loads over the course of many years. The results of this study suggest that deficits in height are not due to single events, but accumulate over many years, since they are more pronounced at older ages.

In the final part of this study, we found that the trade-off between growth and IgE is influenced by family members. Older adults cause increases in both branches, consistent with a role as providers of energy, and children decrease growth but increase IgE, suggesting that children influence relative allocations. In addition to the support these findings give for general hypotheses about humans as cooperative breeders, these findings suggest that life history models may need to be modified to incorporate the effects of reproductive rates and alloparenting on pathogen transmission, along with the corresponding effects disease transmission has on the allocation of energy towards maintenance costs.

BRIDGE TO CHAPTER VI

This chapter has presented research that ties together threads begun throughout this dissertation, by examining growth, immune function, and family composition as parts of a single immune-ecology. In the next chapter I further develop the connections between the studies in this dissertation and present general conclusions from these studies. I present

ideas for future research directions. Finally, I discuss the implications of these studies for the understanding of reaction norms in human adaptability, and the importance of theory in scientific pursuits.

CHAPTER VI

CONCLUSIONS AND FUTURE DIRECTIONS

Changing Circumstances

The Shuar are a lowland indigenous group from Eastern Ecuador. In this dissertation I have reported on fieldwork conducted amongst the Shuar between 2005 and 2009. During this period the changes occurring in market access for many Shuar were obvious even to the casual observer. Several roads were paved across Morona-Santiago, new roads were extended to many Shuar villages, and cell phones became more prevalent with each passing year. Similar changes are occurring in indigenous populations across the globe. The challenge for anthropologists, demographers, and medical workers is to understand these changes as they occur. Studies, such as those reported in Chapters II and III, suggest that market integration can have both positive and negative effects on health and well-being. From a humanitarian standpoint, understanding how economic development and modernization affect health is therefore a critical first step towards improving health.

From a theoretical standpoint these circumstances also provide an opportunity to learn about the adaptability of the human phenotype. Increasing evidence suggests that human life histories and physiologies show substantial dynamic heterogeneity. However,

as the world becomes increasingly homogenized and sanitized we risk missing an opportunity to observe this heterogeneity and risk reaching biased conclusions about human biology based only on data from Western populations. Such biased conclusions can lead to incorrect conclusions about health in the present, such as the conclusion that CRP is always associated with cardiovascular disease (Gurven *et al.*, 2009), or the assumption that IgE levels under 200 IU/ml are "normal" (Janeway, 2005). They can also bias our view of the past. The conditions experienced by forager populations such as the Shuar are clearly not perfectly analogous to the conditions experienced by human ancestors in the distant past. Yet, neither are the conditions experienced by Western populations. By examining the range of the human phenotype across populations, and by understand the reaction norms governing adaptability to diverse environments, we can gain a clearer picture of the range of likely conditions under which humans evolved.

Dynamic Heterogeneity and Human Life Histories

Throughout this dissertation I have examined human life history trade-offs as they are reflected in multiple measures of growth and immune function. In this dissertation I have examined trade-offs between height and weight, between inflammation and humoral immunity, between growth and immunity, and between quantity and quality of offspring. The results support the conclusion that the human phenotype is highly adaptable.

Yet the variation in human phenotypes is clearly non-random. In Chapter II I examined the tradeoff between height and weight. The Shuar follow a pattern common to South America, in that they have a high prevalence of stunting and low prevalence of

wasting. In Chapter III I showed that family members have an effect on height, weight, and caries, and that the effects of family members vary with geographical location. In Chapter V I replicated these findings, but also established that family members have further effects on levels of IgE and CRP.

Overall, the variation in phenotypes appears to follow an adaptive pattern. That is, rather than being simply varying randomly or simply being the product of constraints, energy appears to be directed according to a series of "rules" or reaction norms. Among South American's growth in weight is clearly more protected than growth in height. Height is much more impacted by factors such as energy availability and trade-offs with disease resistance than is weight. The trade-off between inflammation and humoral immunity also appears to represent the early tuning of immune responses with lifelong consequences (Chapter V). Thus, energy does not appear to be generally reallocated, but reallocated in specific ways that likely have adaptive consequences.

This is consistent with the results of other studies. For example, children who are malnourished often show reduced immune response, making vaccines less effective. At the same time, malnourished children may allocate greater *relative* amounts of energy towards immunity, as is indicated by the response of their white blood cells when activated in culture (Azevedo *et al.*, 2005).

At the same time there are clearly aspects of variation that are emerge from the local dynamics of disease transmission. Chapter IV examined the age patterning of IgE in three populations, and found evidence for a shift in the age at which IgE peaks. IgE reaches a peak at earlier ages in populations experiencing higher pathogen loads. This is

likely to have effects on the development of immune function in individuals that are adaptive—by shifting energy into immune function in more individuals at an earlier age. However, the actual peak is a characteristic of the population rather than the individual, and does not mean that all individuals are peaking at the same time or that the age itself is somehow the optimum age at which to shift allocations. Similarly, although caries might be more common if immune function is compromised, it is difficult to imagine that the more than a small portion of the effects on caries discussed in Chapter III represent an adaptive reallocation. It seems much more likely that they result from consumption of market goods containing refined sugars

Future Directions

The studies discussed in this dissertation represent some of the first to examine trade-offs between growth and multiple measures of immune function in a forager population. However, immunoecology and immunoepidemiology are still young disciplines and there are many more questions than there are answers. What are the physiological processes underlying life history trade-offs? Many studies point to hormones as regulators of life histories, yet this is a bit like saying that telephones are the regulators of teenage social lives. Hormones are cellular messengers, and so by definition they are involved in regulating organism wide processes. Similarly, genes are obviously important, but genetic differences between individuals are unlikely to regulate dynamic changes in life histories. More likely most of the variation comes from genetic-based reaction norms that are species or at least population universal. There is also an

increasing appreciation for the importance of epigenetic effects on life histories and phenotypes (Jablonka & Lamb, 2005). The trick is to understand how and why gene expression is regulated, what messages hormones carry and how those messages interact, and how the internal immune-endocrine-ecology is coupled with the exterior social and environmental ecology of human lives.

The measures of immune function used in these studies are somewhat crude. They were selected because of their general applicability, common usage in many populations, and the ease with which they could be applied to a population sample in a field setting. There are many additional markers that would likely provide useful information about the function and development of immune function. These include counts of T-cell sub-types, cytokines, measues of specific antibodies and direct estimation of helminth loads through egg counts. In addition, the studies presented here are cross-sectional. While cross-sectional studies are much easier and cheaper to complete, they sometimes lead to misleading conclusions due to confounds such as cohort effects. In order to truly understand individual life history trajectories longitudinal data is needed. Future studies will need to continue the types of analyses completed in this dissertation over a period of many years.

CONCLUSIONS

Evolutionary and life history theory are broad and useful frameworks for understanding the reactions of humans and other organisms to the environments in which they find themselves. As I hope this dissertation has shown, the application of life

history theory to the studies of health, market integration, and social interactions can produce fruitful results in a way that atheoretical research cannot. The use of theory allows for the formulation of specific hypotheses about how human biology and physiology will react to different environments, even when the conditions of those environments are novel. Thus, studies employing theory are more likely to produce useful results than studies searching simply for associations in a haystack.

APPENDIX

SUPPLEMENTAL MATERIAL FOR CHAPTER II

Table A.1. Growth outcome z-scores from WHO growth references

			N	Percent $z \leq -2$	Percent $z \geq 2$	Mean Z-score	S.D.	t*	p**
Shuar	Males	Height-for-age	682	42%	0%	-1.70	1.19	-37.30	<0.01
		Weight-for-age	536	10%	1%	-0.67	1.07	-14.50	<0.01
		BMI-for-age	679	4%	4%	0.38	1.21	8.20	<0.01
		Weight-for-height	385	3%	11%	0.72	1.30	10.82	<0.01
	Females	Height-for-age	617	37%	0%	-1.63	1.16	-35.12	<0.01
		Weight-for-age	492	11%	1%	-0.72	1.04	-15.39	<0.01
		BMI-for-age	617	2%	3%	0.27	1.00	6.56	<0.01
		Weight-for-height	371	3%	7%	0.44	1.24	6.88	<0.01
Shiwiar	Males	Height-for-age	13	0%	8%	-0.62	1.14	-1.96	0.07
		Weight-for-age	19	5%	0%	-0.24	1.10	-0.95	0.35
		BMI-for-age	12	8%	8%	0.61	1.12	1.89	0.09
		Weight-for-height	3	0%	0%	0.74	0.44	2.93	0.10
	Females	Height-for-age	8	25%	0%	-1.37	1.00	-3.88	0.01
		Weight-for-age	7	0%	14%	0.36	1.01	0.94	0.39
		BMI-for-age	8	0%	0%	0.77	0.86	2.52	0.04
		Weight-for-height	4	0%	25%	1.56	0.56	5.56	0.01
Colono	Males	Height-for-age	315	16%	1%	-0.88	1.09	-14.34	<0.01
		Weight-for-age	263	7%	5%	-0.20	1.26	-2.56	0.01
		BMI-for-age	302	6%	11%	0.35	1.51	3.98	<0.01
		Weight-for-height	130	2%	12%	0.56	1.35	4.70	<0.01
	Females	Height-for-age	243	18%	0%	-0.99	1.11	-13.93	<0.01
		Weight-for-age	192	9%	2%	-0.38	1.14	-4.57	<0.01
		BMI-for-age	231	5%	5%	0.16	1.23	1.95	0.05
		Weight-for-height	111	4%	4%	0.27	1.18	2.44	0.02

*A one-sample t-test was used to determine whether mean z-scores differed significantly from zero. **P-values are 2-tailed

Table A.2. Prevalence of low height-for-age (stunting), low weight-for-age, low BMI-for-age, and low weight-for-height (wasting) in Shuar, Shiwiar, and *Colono* children, by age group, based on WHO references

			Height-for-age			Weight-for-age			BMI-for-age			Weight-for-height		
		Age Cohort	N	% z≤-2	Mean z-score	N	% z≤-2	Mean z-score	N	% z≤-2	Mean z-score	N	% z≤-2	Mean z-score
Shuar	**Male**	**≤5**	31	39%	-1.31	32	13%	-0.69	31	10%	0.23	31	10%	-0.03
		5-9.9	429	36%	-1.57	424	9%	-0.63	427	3%	0.56	336	3%	0.76
		≥10	222	54%	-2.00	80	15%	-0.88	221	5%	0.06	16	0%	1.50
	Female	**≤5**	22	41%	-1.64	24	21%	-0.89	22	0%	0.39	22	0%	0.22
		5-9.9	396	34%	-1.54	396	10%	-0.70	396	3%	0.32	331	3%	0.41
		≥10	199	43%	-1.82	72	10%	-0.81	199	2%	0.14	15	0%	1.43
Shiwiar	**Male**	**≤5**	1	0%	-0.32	-	-	.	-	-	.	-	-	.
		5-9.9	9	0%	-0.67	17	6%	-0.35	9	11%	0.52	3	0%	0.74
		≥10	3	0%	-0.57	2	0%	0.71	3	0%	0.89	-	-	.
	Female	**≤5**	-	-	.	1	0%	2.28	-	-	.	-	-	.
		5-9.9	4	25%	-1.33	5	0%	0.24	4	0%	1.36	4	0%	1.56
		≥10	4	25%	-1.40	1	0%	-0.96	4	0%	0.17	-	-	.
Colono	**Male**	**≤5**	15	13%	-1.00	15	0%	-0.15	15	0%	0.73	15	0%	0.67
		5-9.9	224	13%	-0.75	217	7%	-0.21	218	6%	0.31	114	3%	0.53
		≥10	76	25%	-1.27	31	3%	-0.18	69	6%	0.37	1	0%	1.94
	Female	**≤5**	11	18%	-0.90	11	0%	-0.04	11	0%	0.72	11	0%	0.71
		5-9.9	164	13%	-0.79	153	9%	-0.33	153	4%	0.12	98	4%	0.17
		≥10	68	28%	-1.49	28	18%	-0.74	67	8%	0.14	2	0%	3.16

Table A.3. Child-juvenile (age 3-10) mean growth velocities

HEIGHT		Velocity (cm/year)	SE	95% Confidence Interval Lower	Upper
Shuar	Males	4.77	0.15	4.47	5.06
	Females	4.95	0.16	4.64	5.26
Shiwiar	Males	5.48	1.10	2.99	7.96
	Females	4.83	1.55	-1.84	11.50
Colono	Males	5.31	0.20	4.90	5.71
	Females	5.13	0.22	4.69	5.56

WEIGHT		Velocity (kg/year)	SE	95% Confidence Interval Lower	Upper
Shuar	Males	2.05	0.08	1.88	2.21
	Females	2.17	0.09	2.00	2.35
Shiwiar	Males	2.12	0.64	0.77	3.47
	Females	1.61	0.27	0.87	2.35
Colono	Males	2.43	0.18	2.07	2.78
	Females	2.30	0.19	1.92	2.68

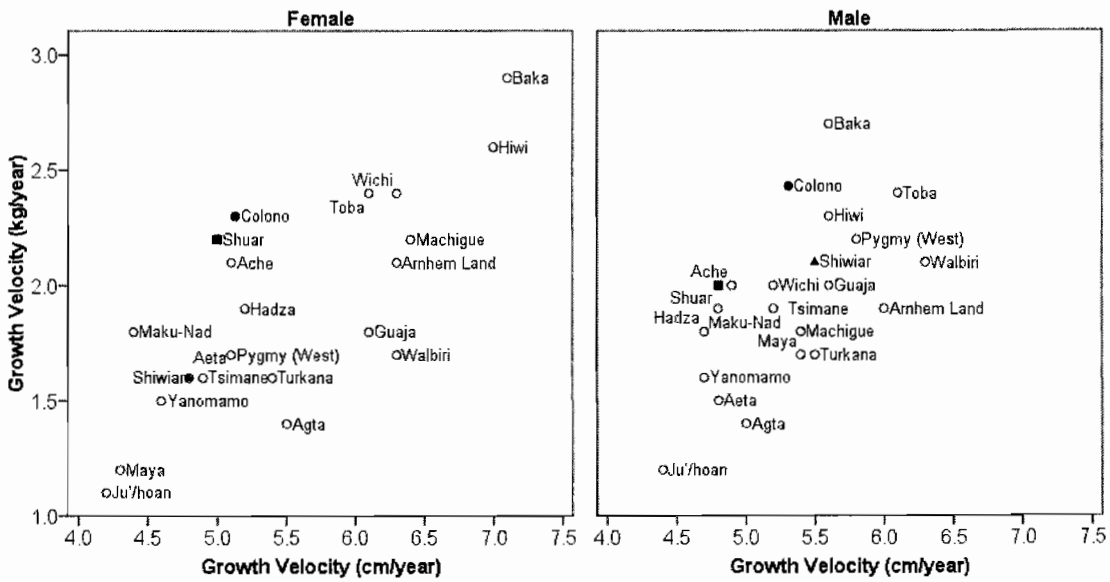

Figure A.1. Female and male height and weight growth velocities for Shuar (dark square), Shiwiar (dark diamond), and *colonos* (dark circle), relative to growth velocities for other indigenous groups. Data for groups other than Shuar, *colono*, and Shiwiar are from Walker, *et al* (2006).

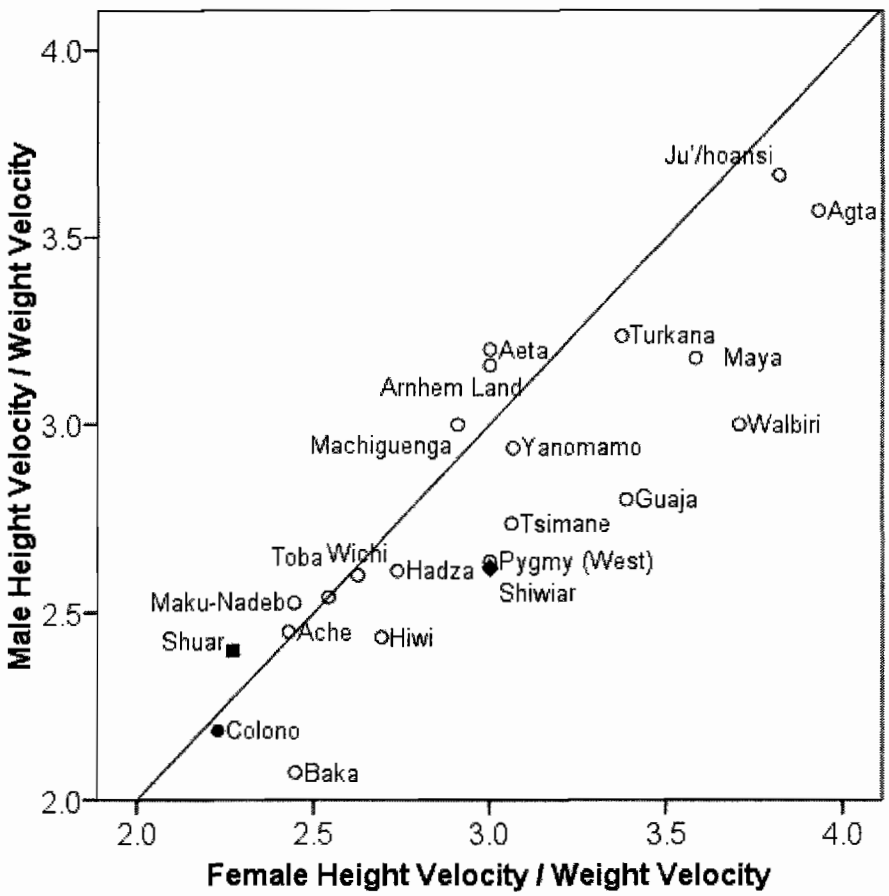

Figure A.2. Ratio of height velocity to weight velocity for both male and female Shuar (dark square), Shiwiar (dark diamond), and *colonos* (dark circle), relative to growth velocity ratios for other indigenous groups. Data for groups other than Shuar, Shiwiar, and *colono* are from Walker, *et al* (2006).

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