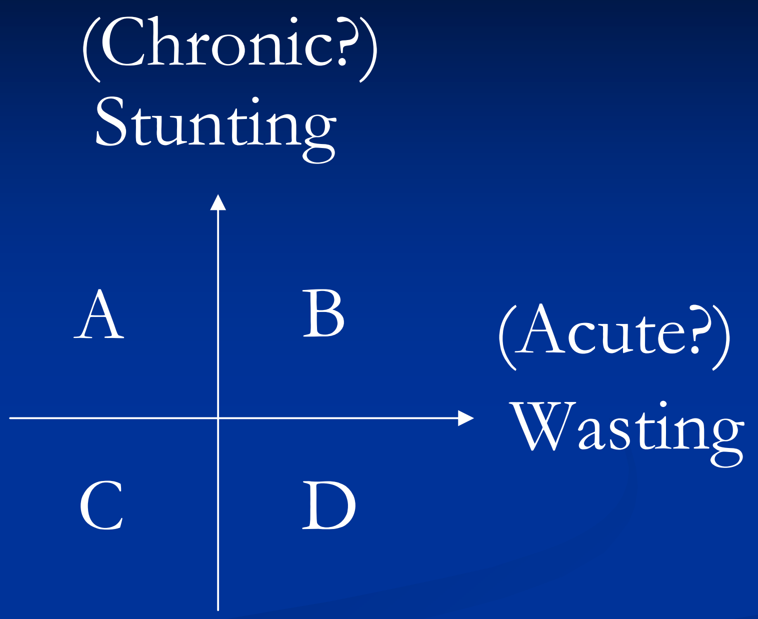
Question:

1. Poor diet throughout the life
2. Well-nourished throughout the life
3. Basically well-nourished, but experienced disaster-related poor diet just recently
4. Gradual improvement of diet throughout the life
2. Gradual degradation in diet throughout the life



In many populations in developing countries,
We have frequently observed:

Why? - Difference in standard growth curve?
Why only height but not weight?

Predictors of C-reactive protein in Tsimane' 2 to 15 year-olds in lowland Bolivia

T.W. McDade[1*], W.R. Leonard[1], J. Burhop[1], V. Reyes-García[2], V. Vadez[2], T. Huanca[2], R.A. Godoy[2]

[1]Laboratory for Human Biology Research, Department of Anthropology, Northwestern University, Evanston, Illinois 60208
[2]Sustainable International Development Program, Heller School for Social Policy and Management, Brandeis University, Waltham, Massachusetts 02454

American Journal of Physical Anthropology, 128: 906-913, 2005.

Abstract. Infectious disease is a major global determinant of child morbidity and mortality, and energetic investment in immune defenses (even in the absence of overt disease) is an important life-history variable, with implications for human growth and development. This study uses a biomarker of immune activation (C-reactive protein) to investigate an important aspect of child health among the Tsimane', a relatively isolated Amerindian population in lowland Bolivia. Our objectives are twofold: 1) to describe the distribution of CRP by age and gender in a cross-sectional sample of 536 2-15-year-olds; and 2) to explore multiple measures of pathogen exposure, economic resources, and acculturation as predictors of increased CRP. The median blood-spot CRP concentration was 0.73 mg/l, with 12.9% of the sample having concentrations greater than 5 mg/L, indicating a relatively high degree of immune activation in this population. Age was the strongest predictor of CRP, with the highest concentrations found among younger individuals. Increased CRP was also associated with higher pathogen exposure, lower household economic resources, and increased maternal education and literacy. The measurement of CRP offers a direct, objective indicator of immune activation, and provides insights into a potentially important pathway through which environmental quality may shape child growth and health. Am J Phys Anthropol., 2005

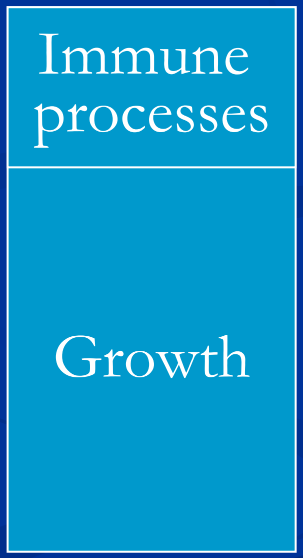
Introduction (1/6)

Infectious diseases → activation of immune processes

Growth faltering:

- Acute/severe → yes
- <u>Chronic/mild → yes?</u>

(Campbell et al., 2003; Solomon et al., 1993)



Proximate determinants of infection

- hygiene
- vaccination
- nutritional status

↑ *embedded*

Transition in ecological/sociocultural/economic/political factors

↑

Globalization/modernization/acculturation

Conventional methods for the evaluation of "infection"

→ Care-giver's report (e.g., 14 days)

- ○ inexpensive, convenient
- × subjective, underreporting, subclinical infectious processes

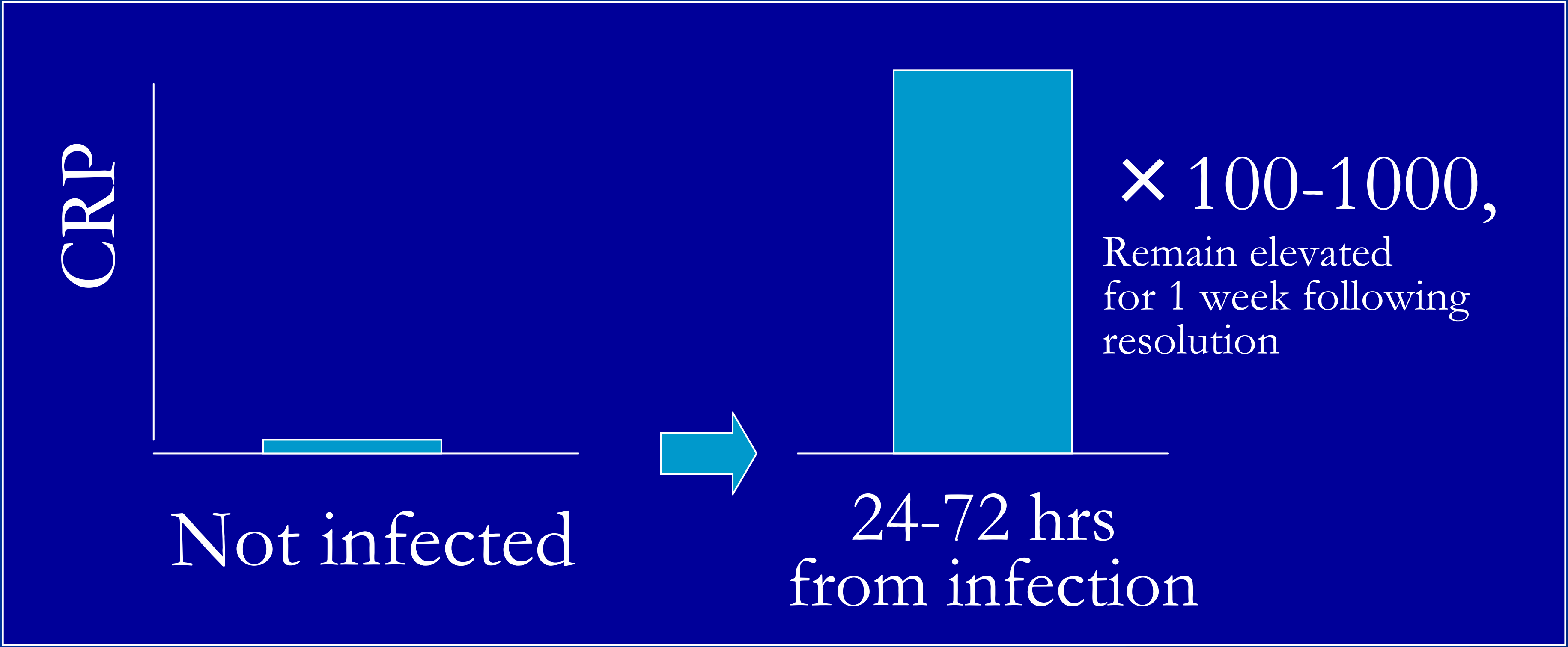
→ Physical examinations

- ○ objective
- × time intensive subclinical infectious processes

CRP (C-reactive protein)

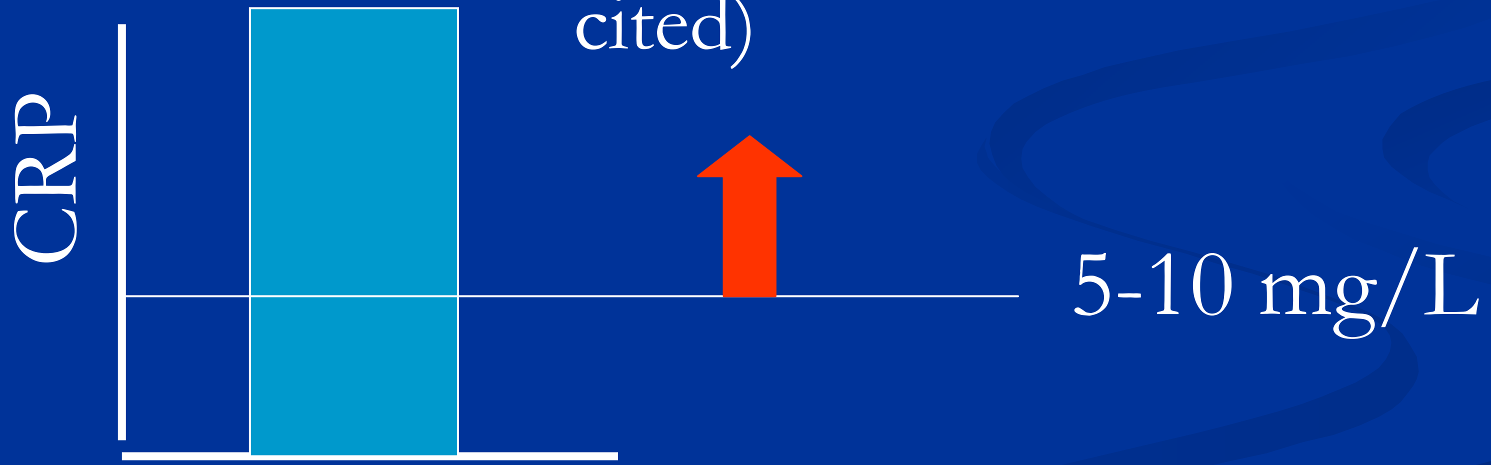
-Central component of acute phase response to infection

-Non-specific systemic response to infection pathgens



Interleukin-6 is primarily responsible for upregulating hepatocyte production of CRP (Ballou and Kushner, 1992; Baumann and Gauldie, 1994; Fleck, 1989).

Infection and inflammatory processes in field-based studies with infants, children and adolescents (e.g., Campbell et al., 2003; 5 more papers are cited)



The objectives:

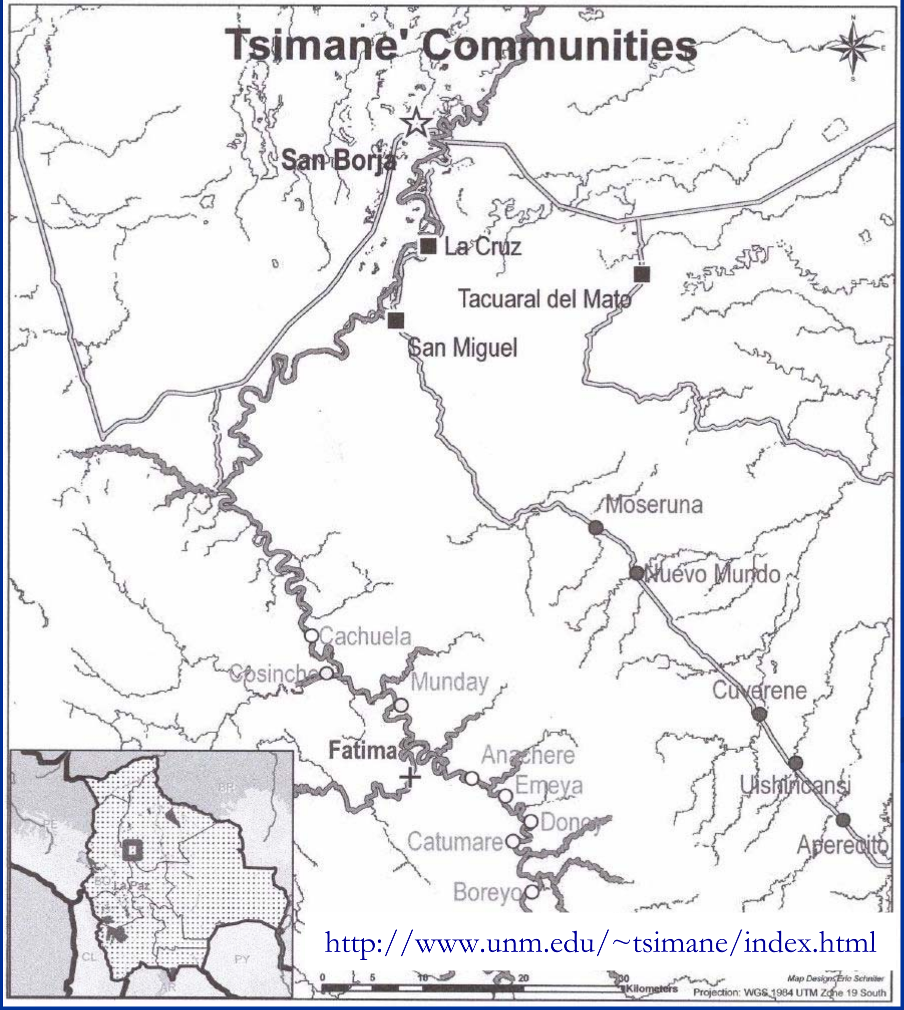
1) to describe the distribution of CRP by age and gender in a population of 2 to 15 year-olds in lowland Bolivia;

2) to investigate the association between cultural and economic transitions and increased CRP.

Method ()

Subjects: Tsimane', an Amerindian population in the Bolivian Amazon

-slush-and-burn farming
-hunting, gathering, wage labor, selling crops
-lowland (urban) and highland (rural)
-no electricity, no running water
-two communities were inaccessible by road



http://www.unm.edu/~tsimane/index.html

Data collection:

<u>Setting:</u>

-12 communities along the Maniqui River

-Varied distance from urban area

<u>Participants:</u>

-Every resident over 2 years who was present

<u>Data:</u>

-Anthropometry (ref: CDC/WHO 1978)

-Questionnaire (HH/Individual level variables)

-Filter blood

(1) Schleicher and Schull No 903

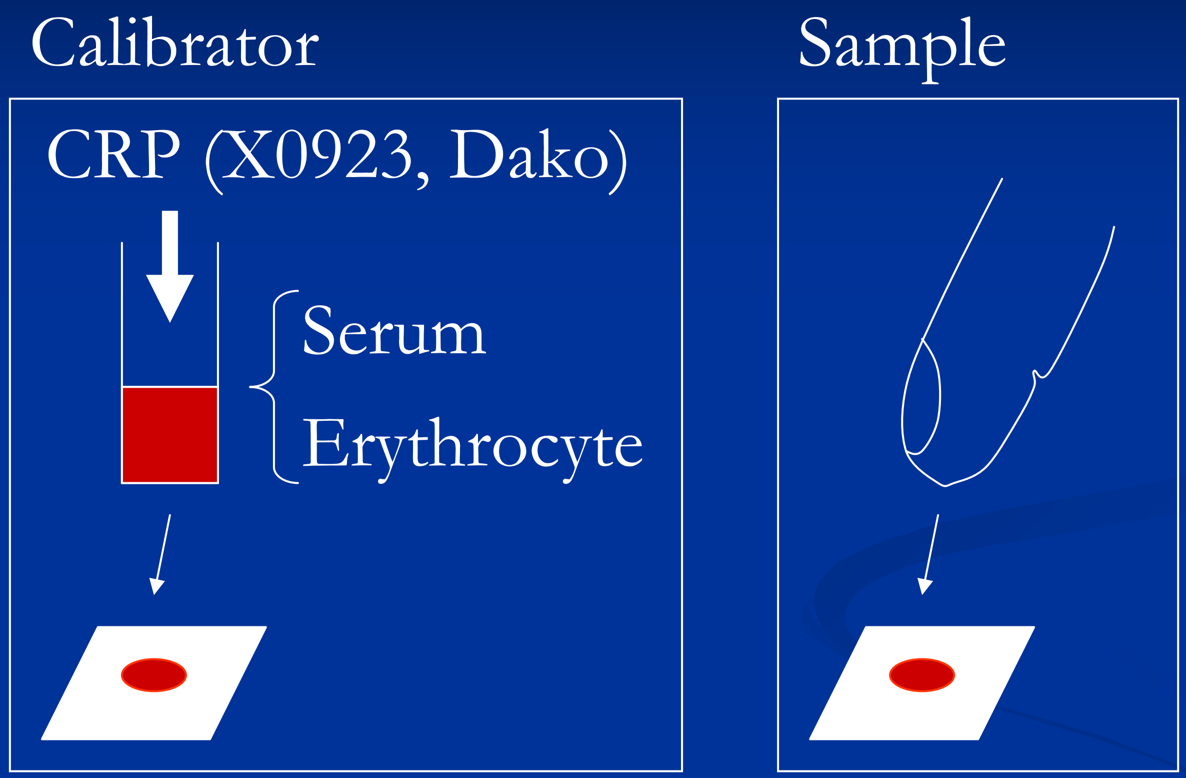
(2) Frozen at 30°C

(3) <3days exposure to tropical temperatures

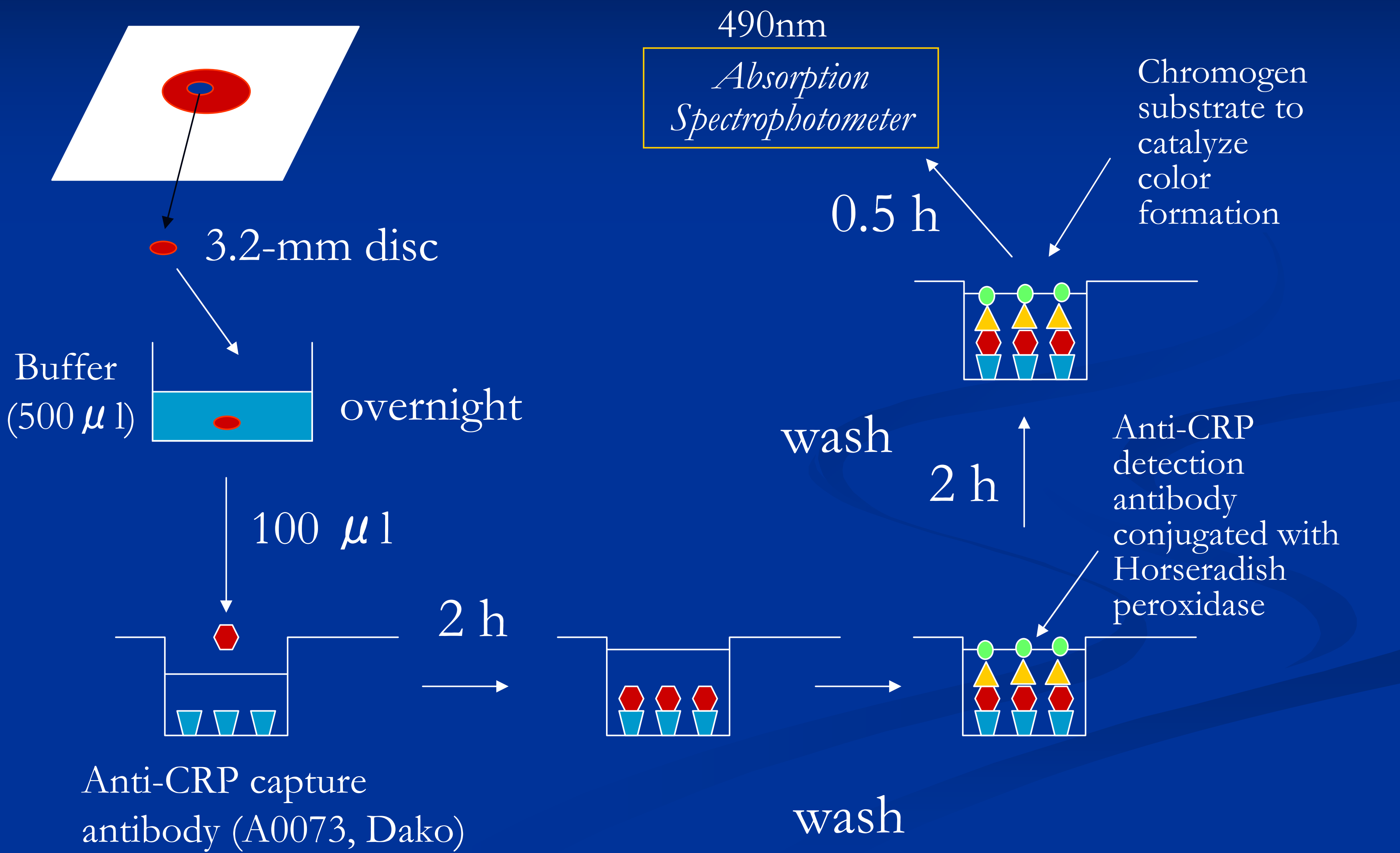
Questionnaire (HH/Individual level variables)

1. Age, gender
2. Pathogen exposure
   (e.g., school attendance, source of water)
3. Economic resources and activities (father, mother)
   (e.g., modern wealth, traditional wealth, "animal" wealth, income from waged labor, income from barter)
4. Accultratiuon
   (e.g., literacy, schooling, writing ability of Spanish, distance to San Borja)

Laboratory analysis of CRP (1)



Laboratory analysis of CRP (2)



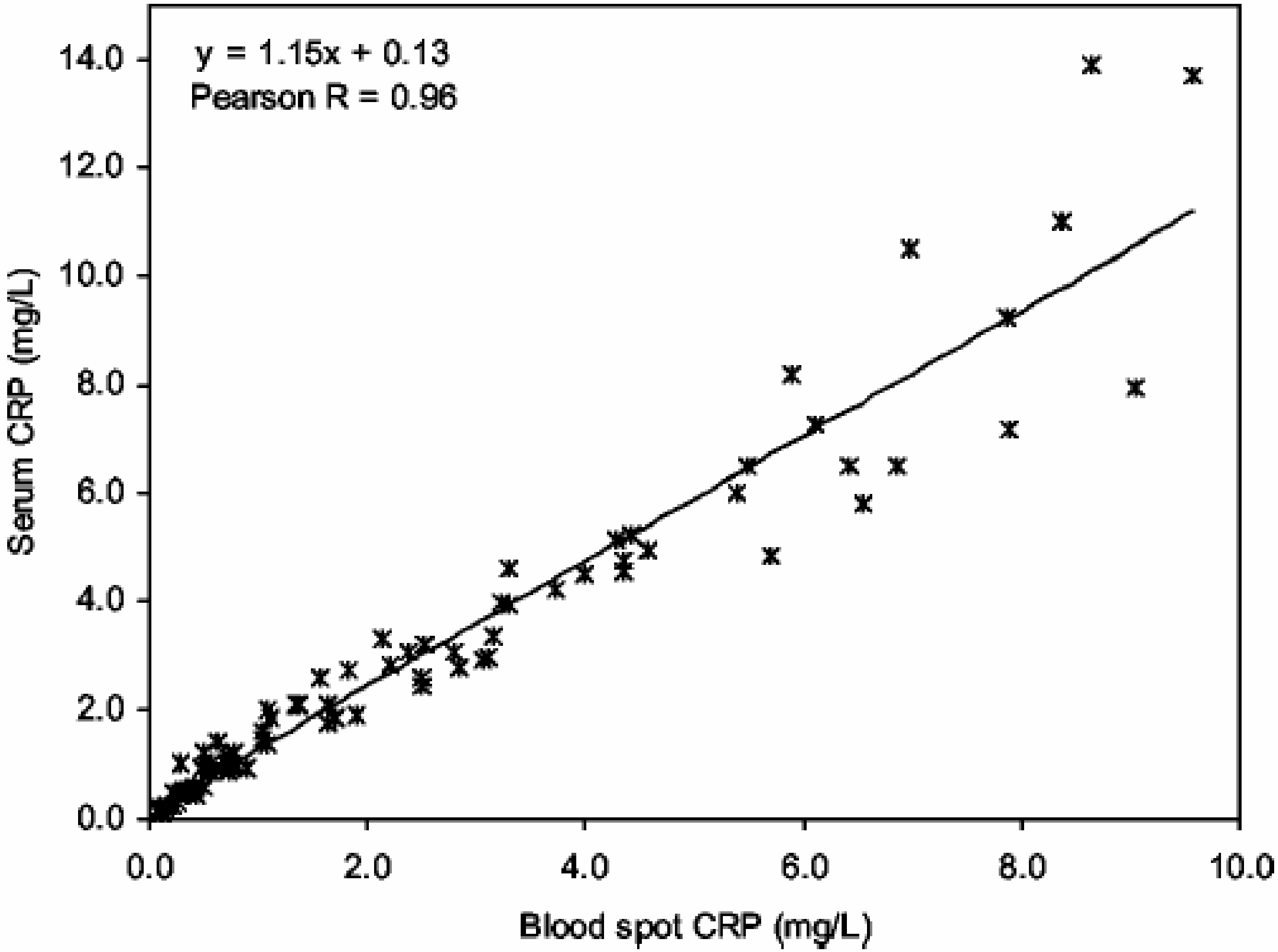


Fig. 1. Relationship between blood-spot and serum CRP concentrations in 84 paired samples.

The best-fit linear regression line is shown. Samples above the highest blood-spot calibrator (10.13 mg/L) are not included (n = 10).

Results (1): Distribution of elevated CRP by age and sex

TABLE 1. Prevalence of elevated CRP and mean (standard deviation) z-scores for height-for-age (HAZ), weight-for-age (WAZ), and weight-for-height (WHZ) by age group

Age (years)	N	% female	% CRP >5 mg/L	HAZ	WAZ	WHZ
2.0–3.9	86	53.5	23.3	−1.90 (1.11)	−0.99 (1.01)	0.23 (0.95)
4.0–5.9	99	45.5	15.2	−1.73 (1.70)	−0.75 (1.28)	0.41 (1.12)
6.0–7.9	94	44.7	10.6	−1.59 (1.35)	−0.74 (1.11)	0.44 (0.91)
8.0–9.9	91	39.6	12.1	−1.75 (1.29)	−0.98 (0.88)	0.49 (0.86)
10.0–11.9	71	45.1	9.9	−1.53 (0.95)	−0.91 (0.77)	
12.0–13.9	58	48.3	8.6	−1.63 (0.87)	−0.73 (0.76)	
14.0–15.9	37	64.9	2.7	−1.66 (0.61)	−0.64 (0.71)	
Total	**536**	**47.2**	**12.9**	**−1.69 (1.25)**	**−0.84 (1.00)**	**0.40 (0.97)**

-%CRP>5mg/L = 12%

-High levels of stunting, little evidence of wasting

-No sex difference in nutritional status

-%CRP>5mg/L was associated with age

Results (1): Distribution of elevated CRP by age and sex

Female

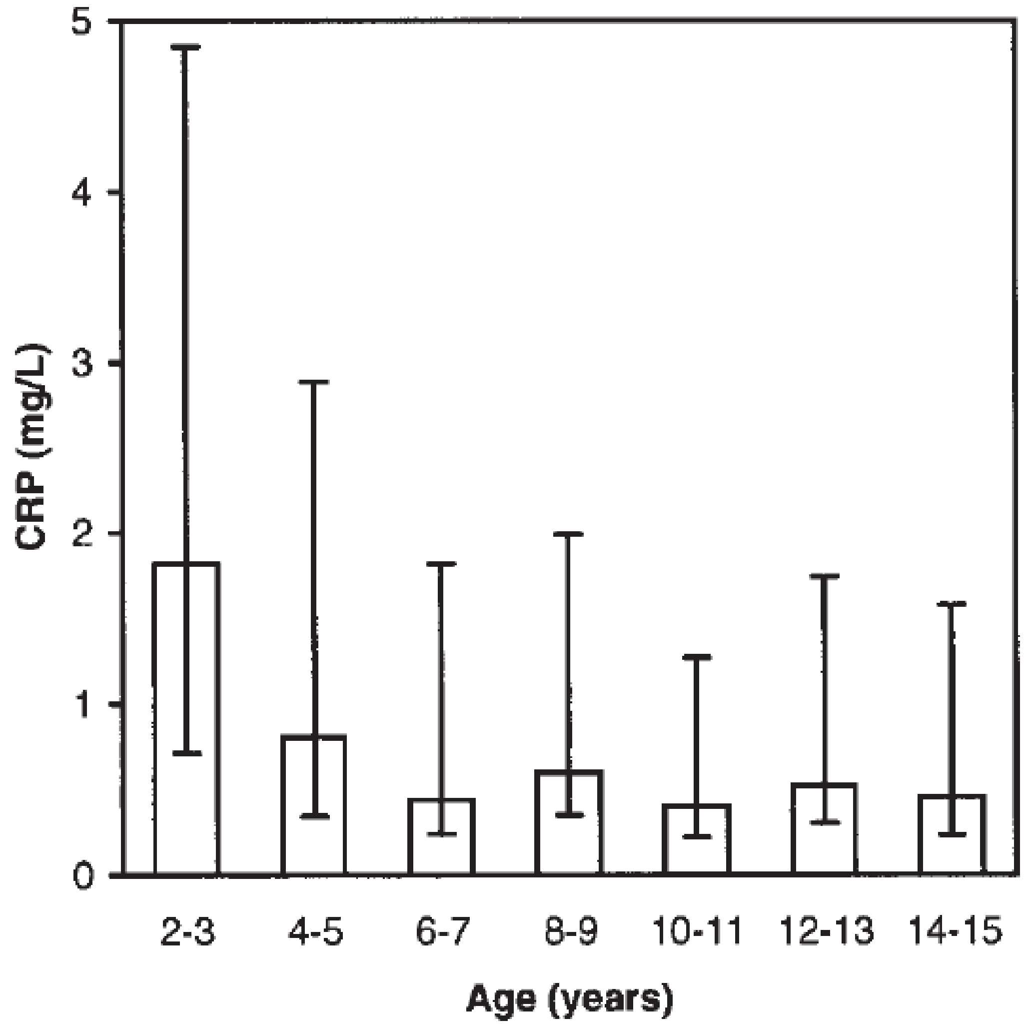


Fig. 1. Median (interquartile range) CRP concentration with age (girls).

Results (1): Distribution of elevated CRP by age and sex

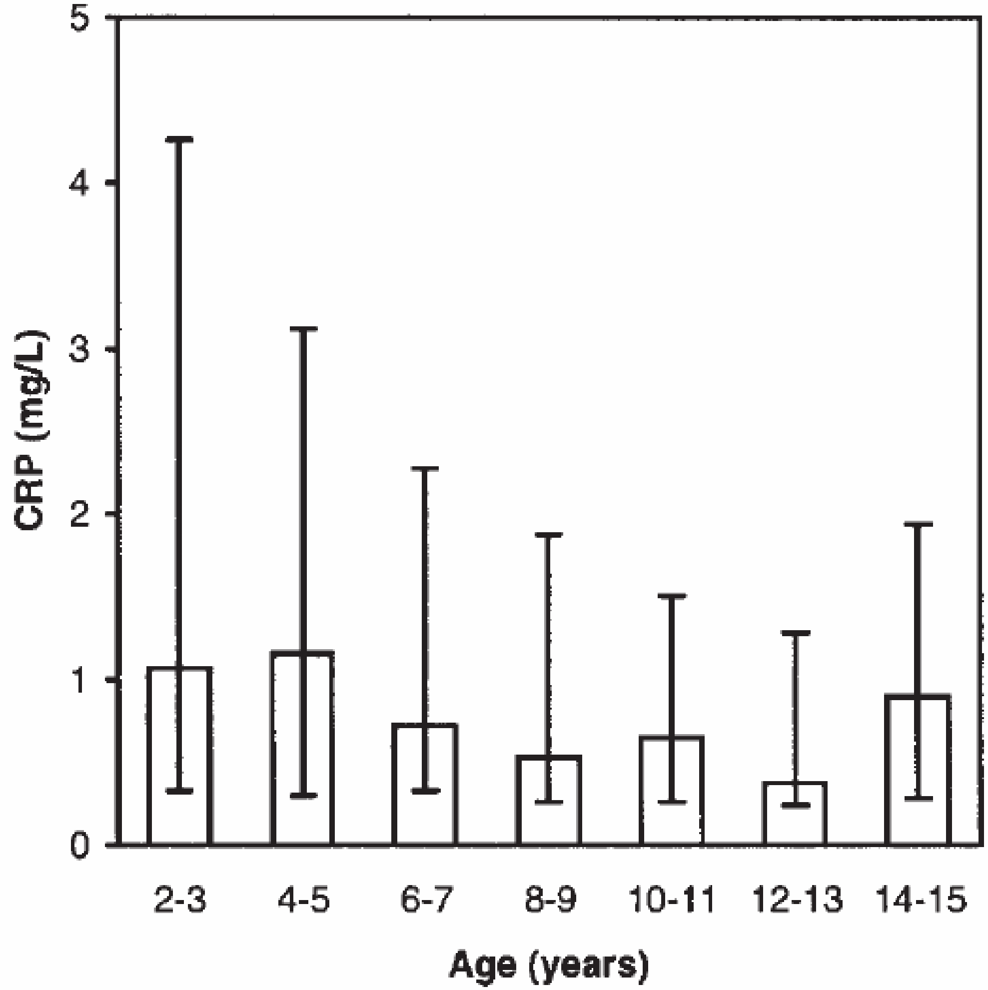


Fig. 2. Median (interquartile range) CRP concentration with age (boys).

Male

Results (2): Measures of pathogen exposure

75.5% of 5-15 years attended school

↓

CRP?

Age × school

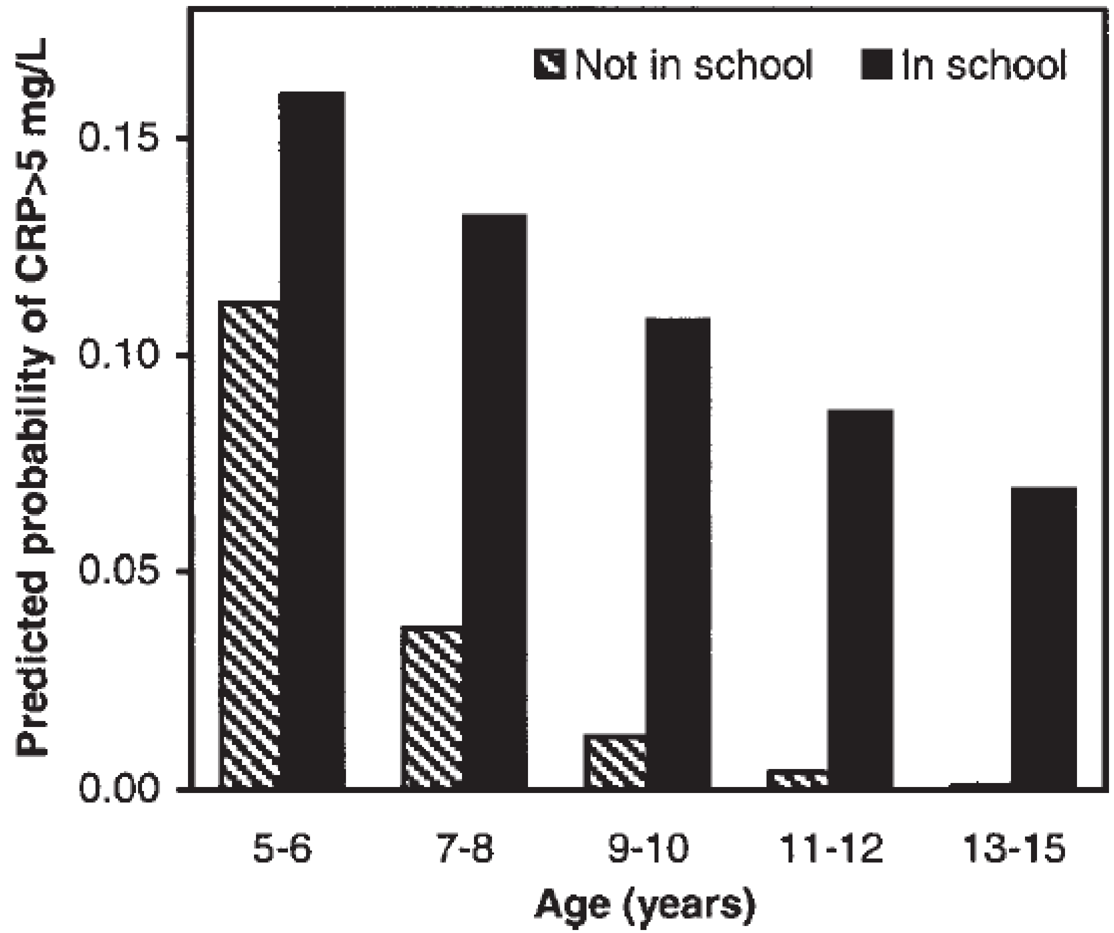


Fig. 3. Predicted probability of CRP >5 mg/L according to age and school attendance for 5–15-year-olds.

Logistic regression model, adjusted by sex

Results (2): Measures of pathogen exposure

35% used river water as primary source

↓

CRP?

OR=2.00, 95%CI: 1.02-3.95

Results (3): Measures of economic resources and activities

Wealth (modern, traditional, animal)
Income over the preceding 2 months
#agricultural plots,

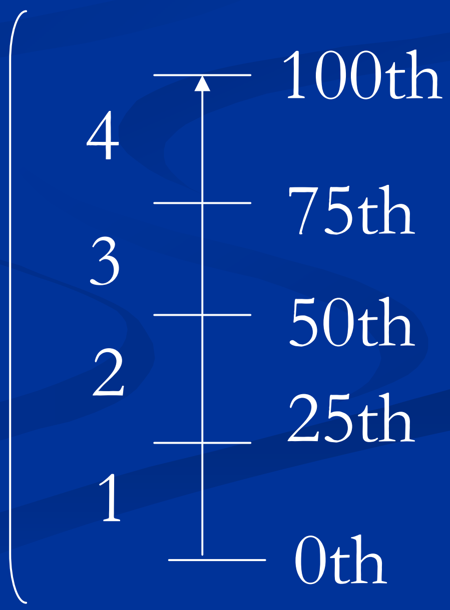
} Factor analysis

↓

1st factor ≒ wealth variable

CRP>5mg/L × wealth variable:
OR=0.83, 95%CI=0.71-0.97
(adj: age, gender, school, river)

←



Income from wage labor
Agricultural plots

} NS

Income from barter: OR=0.78 (P=0.04)

Results (4): Measures of acculturation

Years of schooling (father, mother)
Writing ability (Spanish) (f, m)
Mathematical skill (f, m)
Literacy in Tsimane (f, m)

→ Factor analysis

Factor 1: paternal literacy
(eigen value: 4.25)
Factor 2: maternal literacy
(eigen value=2.45)

CRP × Maternal literacy
OR=1.08, $p=0.022$

CRP × paternal literacy
NS

Results (5): Distance from the commercial center

Distance from San Borja was not associated with CRP>5mg/L

Results (6): Best- and worst-case scenarios

TABLE 2. Maximum likelihood multiple logistic regression model predicting probability of CRP >5 mg/L[1]

Variable	Odds ratio	*P* value	95% confidence interval
School attendance (0 or 1)	0.45	0.203	0.13–1.54
Age (years)	0.70	<0.001	0.62–0.79
School attendance × age	1.29	<0.001	1.12–1.49
River as water source (0 or 1)	2.27	0.028	1.09–4.71
Household wealth (quintiles)	0.86	0.082	0.73–1.02
Value of barter (quintiles)	0.80	0.059	0.63–1.01
Maternal literacy (range, 0–6)	1.09	0.022	1.01–1.17

[1] Log likelihood $= -187.9$, $P < 0.001$, $N = 536$.

Best-case scenario

-not attending school,
-collecting water from sources other than the river,
-a high level of household wealth,
-a high value of bartered goods,
-low maternal literacy

→ **CRP>5mg/L=3%**

Worst-case scenario

-attending school,
-using the river as a primary water source,
-low household wealth,
-low value of bartered goods
-high maternal literacy

→ **CRP>5mg/L=26%**

Discussion (1): evaluation of Tsimane CRP level

Tsimane: median CRP=0.73 mg/L, CRP>5 mg/L=12.9%

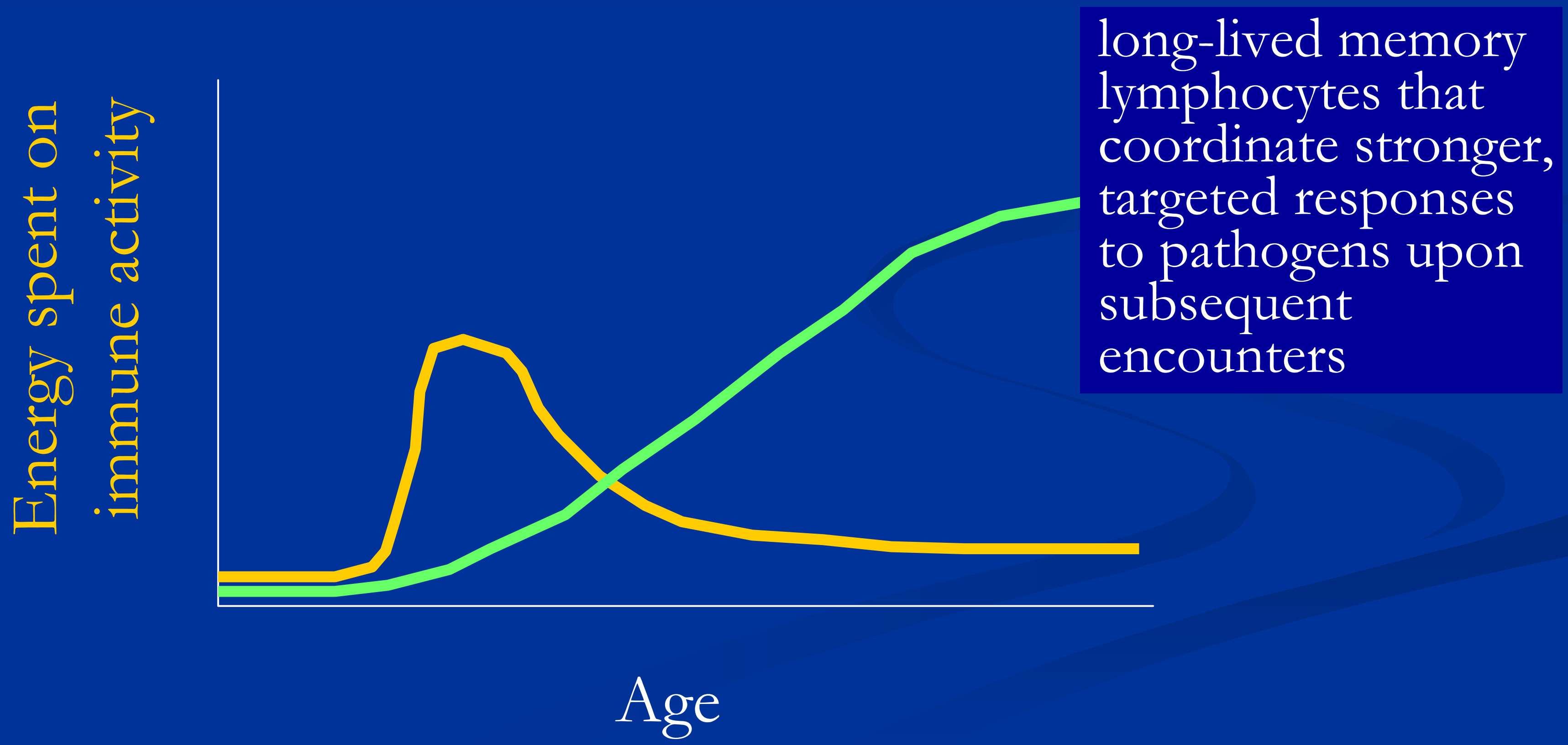
-Samoa (N= 760, 2-20 year): CRP>5 mg/L=6.2%
-England/Wales (10-11 years): plasma CRP=0.14mg/L (25^{th}-75^{th}: 0.06-0.47 mg/L) (Cook et al, 2000)
-NHANES III (8-16 years): beyond detectable concentration of serum CRP (0.22mg/L)=7.1% (males), 6.1% (females)

Plasma/serum CRP>filter blood CRP

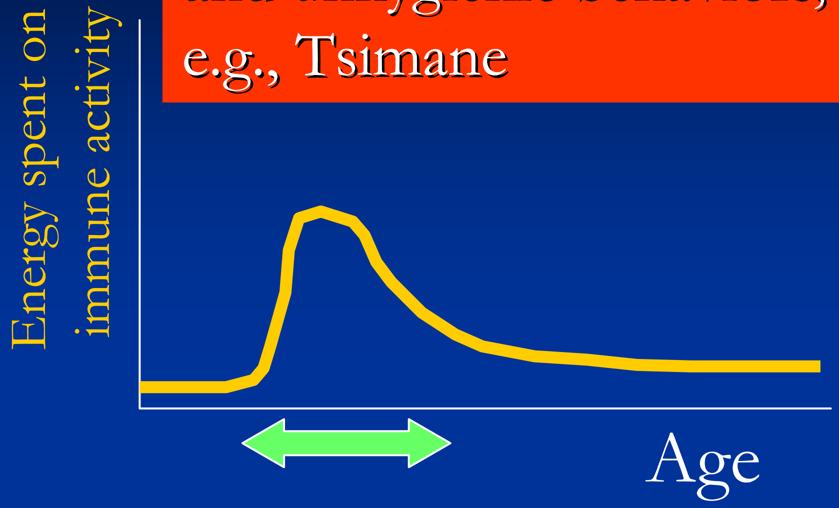
High concentrations of CRP among the Tsimane'
→ high burden of infectious disease, with implications for child growth and overall health?

Discussion (2): higher CRP among younger children

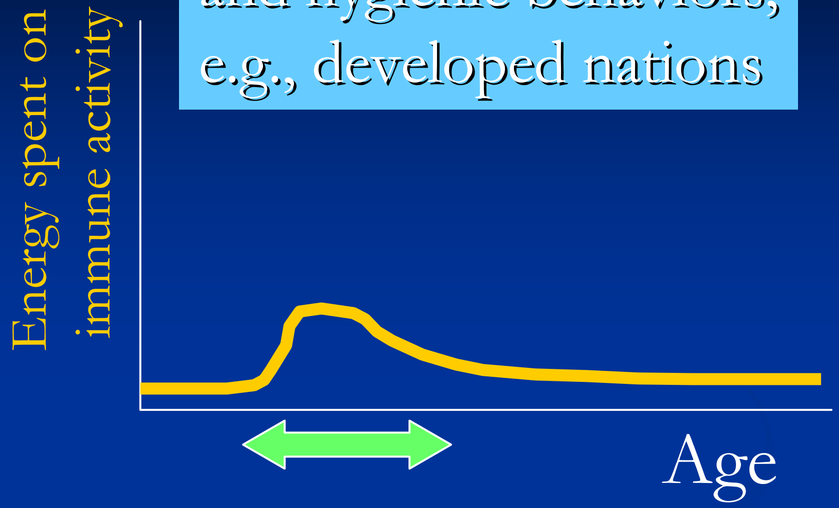
(1) Younger children spend more time in contact with ground
(2) Non-specific, innate immune processes may be more active early in life

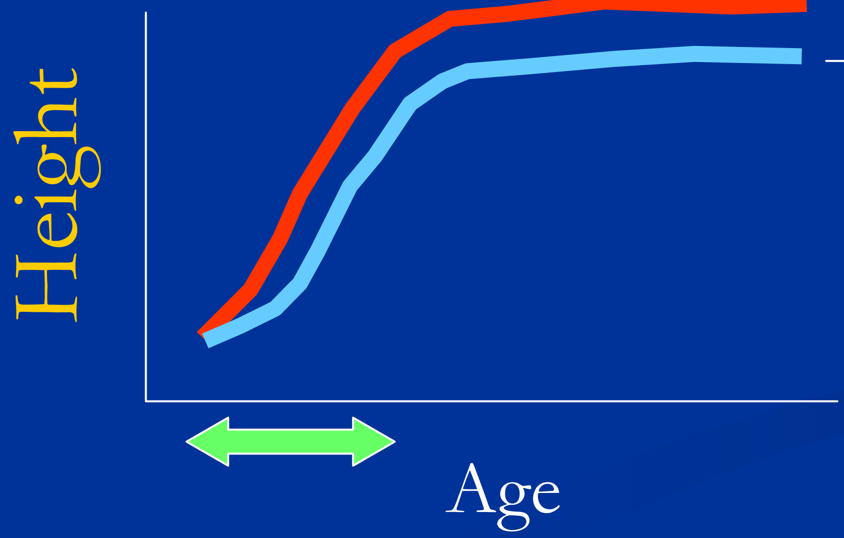


Unhygienic conditions and unhygienic behaviors, e.g., Tsimane



Hygienic conditions and hygienic behaviors, e.g., developed nations





Seriously stunted
Mildly wasted

Discussion (3): higher CRP and highly literacy of mothers

Age of mother × maternal literacy
→ Spearman's R=-0.50, P<0.001

Inexperience of young mothers increased the risk of infection among their children?

Finding in the present study ⟺ large body of literature that suggests that education is positively linked to child health, although the causality of the association has been questioned (Desai and Alva, 1998).

Discussion (5): limitations and further study

CRP at a single time-point:

(1) a contemporaneous acute infection,
(2) recent recovery from acute infection, or
(3) ongoing acute phase activity in response to chronic pathogenic challenge

→ Serial measures of CRP

Acute-phase proteins such as 1-antichymotrypsin as better measures of chronic immunostimulation due to their longer half-life (Calvin et al., 1988).

CONCLUSIONS

We found high concentrations of CRP in Tsimane' children and adolescents, likely reflecting an elevated burden of infectious disease that may contribute to the high degree of growth-faltering in this population. Age was the strongest predictor of increased CRP, with the highest concentrations found in young children. Measures of pathogen exposure, household resources, and maternal literacy were also significant predictors of CRP. Measuring CRP in dried blood spots provides a minimally invasive tool for gaining insights into immune activation and degree of investment in antipathogen defenses, processes that may be particularly important to child growth and health in low-resource settings.