

# Low Serum Insulin in Traditional Pacific Islanders—The Kitava Study

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Increased serum insulin is related to abdominal obesity and high blood pressure in affluent societies where insulin, weight, and blood pressure typically increase with age. The increased insulin level has been thought to reflect insulin resistance, a well-known associated factor in the metabolic syndrome. In most nonwesternized populations, body weight and blood pressure do not increase with age and abdominal obesity is absent. However, it is not known whether serum insulin likewise does not increase with age in nonwesternized societies. Fasting levels of serum insulin were measured cross-sectionally in 164 subsistence horticulturalists aged 20 to 86 years in the tropical island of Kitava, Trobriand Islands, Papua New Guinea, and in 472 randomly selected Swedish controls aged 25 to 74 years from the Northern Sweden WHO Monitoring Trends and Determinants in Cardiovascular Diseases (MONICA) Study. In Kitava, the intake of Western food is negligible and stroke and ischemic heart disease are absent or rare. The body mass index (BMI) and diastolic blood pressure are low in Kitavans. The main outcome measures in this study were the means, distributions, and age relations of serum insulin in males and females of the two populations. Serum fasting insulin levels were lower in Kitava than in Sweden for all ages ( $P < .001$ ). For example, the mean insulin concentration in 50- to 74-year-old Kitavans was only 50% of that in Swedish subjects. Furthermore, serum insulin decreased with age in Kitava, while it increased in Sweden in subjects over 50 years of age. Moreover, the age, BMI, and, in females, waist circumference predicted Kitavan insulin levels at age 50 to 74 years remarkably well when applied to multiple linear regression equations defined to predict the levels in Sweden. The low serum insulin that decreases with age in Kitavans adds to the evidence that a Western lifestyle is a primary cause of insulin resistance. Low serum insulin may partly explain the low prevalence of cardiovascular disease in Kitavans and probably relates to their marked leanness.

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**I**N WESTERNIZED POPULATIONS, peripheral insulin sensitivity decreases with advancing age, which is partly reflected by a gradual increase in serum insulin in the fasting state.<sup>1</sup> In epidemiological surveys, insulin resistance has been associated with abdominal obesity and high blood pressure.<sup>1</sup> In addition, fasting insulin may be an independent risk marker for ischemic heart disease,<sup>2</sup> and hypothetically, insulin resistance is an important cause of cardiovascular disease even in the absence of hypercholesterolemia.<sup>3</sup> Whether insulin sensitivity also decreases with age in populations with a low prevalence of cardiovascular disease is not known.

We have performed a health survey among the people of Kitava in the Trobriand Islands of Papua New Guinea, who are uninfluenced by Western dietary habits and whose staple foods are tubers, fruit, coconut, fish, and vegetables. The population is free from overweight and, apparently, hypertension, cardiovascular disease, and malnutrition.<sup>4,5</sup> In this study, we analyzed the means, distributions, and age relations of fasting serum insulin in this population compared with an age- and gender-matched population of Westerners, in which age-related increased levels have been documented.<sup>6</sup>

## SUBJECTS AND METHODS

The survey received ethical approval by the national Medical Research Advisory Committee of Papua New Guinea. It was approved by other national and provincial bodies and at the community level by the inhabitants and their chiefs. From a total population of 2,300 Kitavans, all subjects older than 50 years ( $n = 206$ ) and 20% of those

aged 20 to 49 ( $n = 41$ ) were eligible. Informed consent was obtained through personal contact. Age was calculated from known historical events and was considered accurate to within 3 years for most subjects. The response rate for serum sampling was only 42%, and therefore, self-selected subjects aged less than 50 years were included. We thus recruited 121 males and 49 females aged 20 to 86 years, of whom 29% were self-selected. A random age- and gender-matched subsample of 472 subjects aged 25 to 74 years from the population-based Northern Sweden WHO Monitoring Trends and Determinants in Cardiovascular Diseases (MONICA) Study (79% response rate) served as controls.<sup>6</sup> In both populations, serum was sampled before 9 AM, after 9 to 15 hours of fasting. The samples were centrifuged within 60 minutes, immediately frozen in liquid nitrogen, and later stored at  $-70^{\circ}\text{C}$  until analysis. The Swedish samples were collected from January to April 1994 and analyzed later that year, while Kitavan samples were collected in late 1990 and analyzed in early 1996.

Serum glucose was determined by the glucose oxidase method and serum insulin by radioimmunoassay (Phadesept Insulin RIA; Pharmacia Diagnostics, Uppsala, Sweden) in the same laboratory for the two populations. Standard methods were used for measurement of sitting blood pressure (mercury sphygmomanometer), weight (single-beam balance scale), standing height (measuring rod), waist circumference (tape measure), triceps skinfold thickness (Harpender caliper), and midarm circumference (tape measure). Clinical characteristics of the two study populations are presented in Table 1.

Kitavan dietary habits were investigated by a diet history, weighing of ready-to-eat foods, and sharing of food habits by one of the authors (S.L.) who lived with the people for 7 weeks,<sup>7</sup> during which time the patterns of physical activity were observed and supplemented with nonsystematic interviews.

Tubers (yam, sweet potato, taro, and manioc), fruit, fish, and coconuts were the dietary staples, and the intake of Western food was negligible. The estimated proportion of energy derived from total, saturated, monounsaturated, and polyunsaturated fatty acids (PUFAs) was 21%, 17%, 2%, and 2% of dietary energy, compared with 37%, 16%, 16%, and 5% in Sweden. Saturated fat intake thus was not different from the intake in Sweden. The intake of n-3 PUFAs, soluble fiber, minerals, and vitamins was high among Kitavans. The median basal metabolic rate (BMR) as predicted from weight at age 18 to 30 years was 5.5 MJ/d in males and 4.9 MJ/d in females.

The level of physical activity of Kitavans was roughly estimated at

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**Table 1. Clinical Characteristics of the Study Populations (mean ± SD)**

Characteristic	Kitava	Sweden	P
<b>Males</b>			
No. of subjects	119	221	
Age (yr)	49 ± 18	53 ± 14	.052
BMI (kg/m <sup>2</sup> )	20 ± 2	26 ± 4	.0001
Waist/height (cm/m)	46 ± 2	53 ± 6	.0001
Systolic BP (mm Hg)	116 ± 15	132 ± 20	.0001
Diastolic BP (mm Hg)	70 ± 6	82 ± 11	.0001
Smoking rate (%)	76	16	.0001
<b>Females</b>			
No. of subjects	41	251	
Age (yr)	51 ± 16	50 ± 14	.5
BMI (kg/m <sup>2</sup> )	18 ± 2	26 ± 5	.0001
Waist/height (cm/m)	46 ± 4	51 ± 8	.0001
Systolic BP (mm Hg)	120 ± 18	128 ± 24	.046
Diastolic BP (mm Hg)	71 ± 7	79 ± 11	.0001
Smoking rate (%)	76	24	.0018

Abbreviation: BP, blood pressure (sitting BP in Kitavans and supine BP in Swedes).

1.7 multiples of BMR. The level for Westerners with a low occupational activity level who are nonactive at leisure time is 1.4-fold BMR for both sexes, while for moderately active individuals at work and during leisure time, the level is 1.7-fold BMR for males and 1.6-fold BMR for females.<sup>8</sup> For 18- to 30-year-old Kitavan males, the estimated energy expenditure was 9.4 MJ, while the estimated total daily caloric intake from the diet history was 9.2 MJ. Energy expenditure decreased with age in both populations. In the Swedish population, self-reported physical activity during work and leisure time were each coded to a three-point scale (low, medium, and high level of physical activity) using a questionnaire.<sup>9</sup>

Three of four Kitavan males and females were daily smokers, and the rest were nonsmokers. The difference in triceps skinfolds and serum lipoproteins and apolipoproteins between smokers and nonsmokers was of the same magnitude as in Western populations.<sup>5</sup> The estimated life expectancy was 45 years at birth and an additional 25 years or more thereafter. Major causes of death were infections, trauma, and complications of pregnancy, whereas atherothrombotic disorders were absent or rare.

Continuous variables were checked for or transformed to apparent normality by repeated use of normal probability plots.<sup>10</sup> After simple logarithmic transformation, serum insulin showed perfectly normal distribution. Strictly from their appearance on the normal plots, four Kitavan outliers were excluded, namely two males and two females with serum insulin of 26.2, 17.8, 17.5, and 30.3 IU/mL. Three of these were incidentally suspected of having eaten prior to sampling. Group means and distributions of serum insulin were compared by the two-sample *T* test. Geometric means (the antilog of the mean of the logarithmically transformed variable) were calculated. A *P* level less than .05 was chosen for statistical significance. Simple and forward stepwise multiple linear regressions were applied with log insulin as the dependent variable. Inclusion of Kitavan outliers did not essentially change the results.

A subsample of Kitavans older than 50 years was further analyzed. This cutoff limit was chosen because of an increase in serum insulin among Swedish subjects above this age.

**RESULTS**

In all age groups, fasting serum insulin and glucose were lower in Kitavans than in Swedish subjects (Table 2 and Fig 1). Adjusting for differences in the estimated level of physical

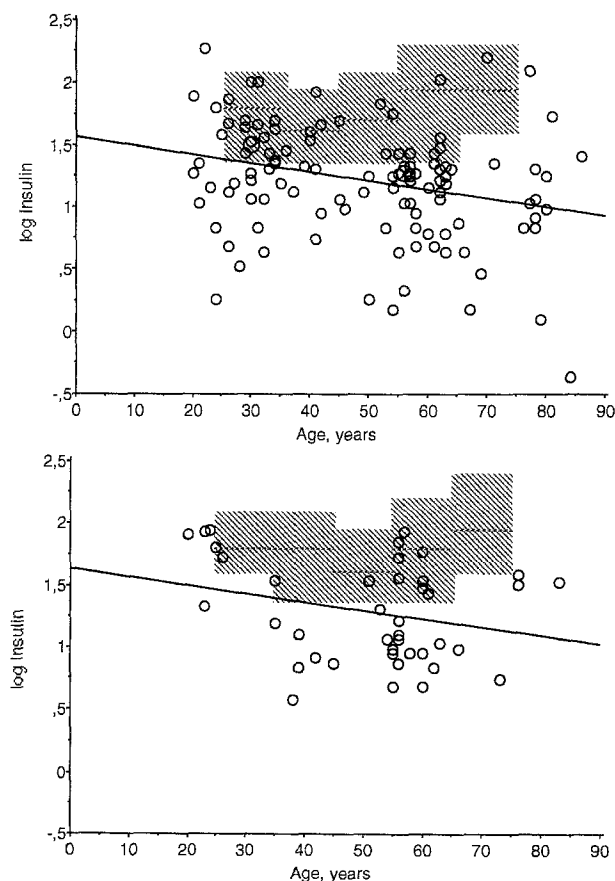
**Table 2. Serum Insulin and Glucose Levels in Kitava and Sweden**

Age Group (yr)	Insulin			Glucose		
	Kitava	Sweden	P	Kitava	Sweden	P
<b>Males</b>						
25-39	3.9 (3-5)	5.7 (4-8)	.0018	3.5 (3.3-3.9)	5.3 (5.0-5.6)	.0001
40-59	3.4 (3-4)	5.9 (4-9)	.0001	3.8 (3.4-4.1)	5.5 (5.2-5.8)	.0001
60-74	3.4 (2-4)	7.5 (5-11)	.0001	3.8 (3.5-4.2)	5.6 (5.1-5.9)	.0001
<b>Females</b>						
25-39	3.5 (2-6)	6.2 (4-8)	.0061	3.5 (3.3-3.8)	4.9 (4.6-5.1)	.0001
40-59	3.8 (3-5)	5.8 (4-8)	.0027	3.8 (3.1-4.5)	5.2 (4.9-5.4)	.0001
60-74	3.7 (2-5)	7.2 (5-10)	.0002	4.3 (4.0-4.5)	5.4 (5.0-5.7)	.0001

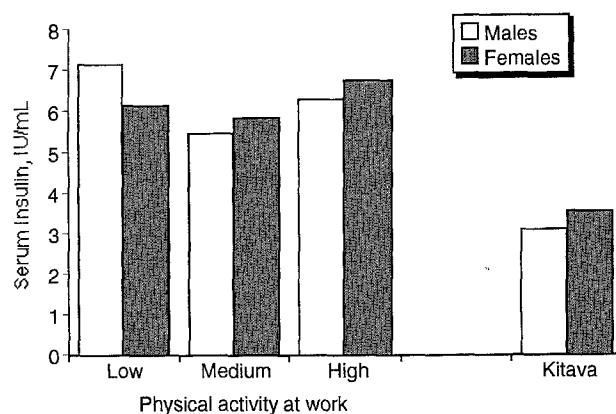
NOTE. Results are the geometric mean (interquartile range) of fasting serum insulin (IU/mL) and glucose (mmol/L). *P*, Student *t* test on log insulin.

activity during daily activities did not essentially change the results, as shown for the age group 50 to 65 years in Fig 2.

In Swedish subjects, serum insulin showed a slightly J-shaped or curvilinear relation with age and an increase after 50 years independently of the body mass index (BMI) and waist circumference. In Swedish males, the age and BMI, and in females, the age, BMI, and waist circumference, were each positively and independently associated with insulin (data not shown). When Kitavan values for the age, BMI, and waist



**Fig 1. Fasting serum insulin in Kitavan males and females. (■) Reference intervals for healthy Swedish subjects, whose lower and upper limits represent the 10th and 90th percentiles, respectively. (---) Swedish medians.**



**Fig 2. Fasting insulin at age 50-65 years at different levels of occupational physical activity in Sweden and Kitava (geometric means,  $P < .0009$  for Kitavans v any Swedish groups).**

circumference were entered into these Swedish regression equations, the predicted geometric means of insulin for Kitavan males and females were 3.12 and 3.29 IU/mL, respectively, while the observed geometric means for Kitavans were 3.08 and 3.37 IU/mL. The observed geometric means of insulin for Swedish males and females were 6.98 and 6.65 IU/mL.

A negative linear relation between insulin and age was present in Kitavan males ( $r = -.27$ ,  $P = .0028$ ), and a similar tendency was noted in females ( $r = -.26$ ,  $P = .10$ ). This decrease in insulin with age was explained in both sexes by a variation in the arm circumference: in forward stepwise multiple linear regression, midarm circumference was positively related to insulin in males ( $P = .017$ ) and tended to be so in females ( $P = .14$ ), while the age, BMI, and waist circumference were not ( $P = .8$  for age forced into the equation). In simple linear regression, midarm circumference was positively related to insulin in males ( $r = .29$ ,  $P = .0020$ ) and tended to be so in females ( $r = .27$ ,  $P = .09$ ). Adjustment for log glucose strengthened the relation between insulin and age in males ( $P = .0003$ ) and weakened it in females ( $P = .4$ ).

## DISCUSSION

The Kitavans provide one of the last opportunities to study humans who are uninfluenced by Western dietary habits. The low fasting insulin concentrations that do not increase with age suggest high insulin sensitivity in this very lean population. In conjunction with a low BMI and diastolic blood pressure,<sup>5</sup> this may partly explain the virtual absence of cardiovascular disease among Kitavans.

We do not consider our findings to be hampered by selection bias. The eligible population is homogeneous and randomized, and nonattending subjects did not differ by appearance in body composition, agility, or level of physical activity. In addition, none of the measured variables differed between randomized and self-selected subjects.

There is little reason to suspect genetics as a major explanation. Compared with populations of northern European ancestry, traditional ethnic groups in general and Pacific Islanders in particular seem more prone, not less, to develop diabetes after adopting a Western lifestyle.<sup>11,12</sup>

As to environmental causes of the low serum insulin in

Kitavans, our methods preclude any detailed speculation on the possible impact of energy balance, fat intake, or other lifestyle factors. Nutritional characteristics of possible importance are that the Kitavan diet is low in energy and fat and is therefore satiating,<sup>13,14</sup> and has a low glycemic index.<sup>15</sup> The very low fat intake in Kitava, about 20% of calories, is potentially important since a high-fat diet may promote insulin resistance.<sup>16-18</sup> Possibly, the high n-3 to n-6 PUFA ratio plays an additional role.<sup>18</sup> In contrast, the notion that high-carbohydrate diets are a cause of insulin resistance<sup>19</sup> is not supported by the low fasting insulin levels in Kitava, where carbohydrate provides an estimated 70% of calories.<sup>7</sup> Possibly, the quality rather than the quantity of carbohydrates is important: carbohydrate-rich foods with a low glycemic index and a high nutrient density, such as Kitavan tubers<sup>20</sup> and fruit, may be preferable to refined cereals and sugar.

The typical level of physical activity in Kitava is fairly high and compares with that of Westerners who are moderately active both at work and during leisure time. The weak relation between physical activity and serum insulin in the Swedes nevertheless suggests that exercise is not the main explanation for the low Kitavan insulin levels. This is in line with research in Westerners suggesting that exercise alone is insufficient to fully prevent insulin resistance.<sup>21</sup>

The remarkable accuracy of Swedish regression equations in predicting mean Kitavan insulin levels from the Kitavan BMI and waist circumference adds to the notion that abdominal obesity is a more important determinant of insulin resistance than aging per se.<sup>22-24</sup>

The age-related decrease of serum insulin in Kitavans was eliminated after adjustment for midarm circumference, which in this lean population probably mainly reflects muscle mass. A positive relation between muscle mass and insulin should not be unexpected, since insulin is needed for glucose uptake into muscle cells. High fasting insulin levels in populations with a low-risk for cardiovascular disease may thus be a marker of increased muscle mass rather than insulin resistance.

This is the first study to compare serum insulin levels across a wide age range between a traditional and a Western population. In three small surveys in young hunter-gatherers (the Yanomama of Brazil, the !Kung San of Botswana, and the Mbuti Pygmies of Zaire), serum insulin was 35% lower in the !Kung San than in Caucasians, while the other two groups showed similar levels as Caucasians.<sup>25-27</sup> Nevertheless, insulin sensitivity seemed high in all three populations, as reflected by a modest increase of blood glucose and serum insulin during the glucose tolerance test.

Despite the limitations of using fasting serum insulin as an index of insulin resistance, at least on an individual level, our findings suggest that insulin sensitivity may be unnaturally low in the majority of middle-aged and elderly Westerners. This, in turn, may be reflected by the increased prevalence of diseases associated with insulin resistance in Western societies, such as the metabolic syndrome. We propose that increasing fasting insulin is not part of normal aging but is rather an untoward effect of a Western diet and lifestyle—in analogy with the typical age-related increase of waist circumference and blood pressure in affluent societies. This study also adds to the growing concern about the epidemic of insulin resistance and cardiovascular disease in developing countries.

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