OBJECTIVE—To evaluate whether fasting plasma glucose (FPG) within a normoglycemic range is associated with cardiometabolic risk factors (CMRF) among children and adolescents in an outpatient setting.

RESEARCH DESIGN AND METHODS—Subjects (780; age 6–16 years) with FPG <100 mg/dL were divided into tertiles of FPG.

RESULTS—BMI, waist circumference, homeostasis model assessment-insulin resistance, systolic blood pressure, and white blood cell (WBC) count (P < 0.001) increased across tertiles of FPG. Subjects with high-normal FPG (89–99 mg/dL) showed a higher risk of insulin resistance, hypertension, and high WBC count compared with subjects with low-normal FPG, independent of BMI z score.

CONCLUSIONS—In outpatient children and adolescents, higher FPG within the normal range is associated with several CMRF, independent of obesity. Thus the simple measurement of FPG may help identify subjects who warrant some monitoring in relation to cardiovascular risk.

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FPG showed an increased risk of IR, hypertension, and high WBC count compared with subjects with low-normal FPG (Table 1). The group with mid-normal FPG, as compared with the low-normal FPG, showed an increased risk of IR and hypertension, but not of high WBC count. These results did not change when the category of overweight/obesity was included in the model instead of BMI z score.

**CONCLUSIONS**—This study demonstrates that in an outpatient setting of normoglycemic Caucasian children and adolescents, FPG is associated with several CMRF, independent of obesity. In adults, a high but normal FPG is a risk factor for development of type 2 diabetes (11) and cardiovascular disease (12). Previous studies exploring the clinical significance of high-normal FPG in children have been performed in obese subjects (4–6). In a sample of 323 obese children, Grandone et al. (5) showed that high-normal FPG (87–99 mg/dL) is associated with a sevenfold higher risk of presenting IGT and IR. More recently, O’Malley et al. (6) reported a reduction in both insulin sensitivity and β-cell function at increasing FPG in normoglycemic multiethnic obese youth, thus demonstrating that some deterioration of glucose homeostasis is already present at apparently normal FPG. Our study extends this observation by demonstrating that FPG is associated with a cluster of CMRF and demonstrates that this relationship is independent of BMI. Actually, subjects with FPG between 89 and 99 mg/dL not only demonstrate that systemic inflammation may appear early in life and be related to subclinical abnormalities of glucose metabolism.

In conclusion, in an outpatient setting of Caucasian children and adolescents, FPG within the normal range is associated with several CMRF, independent of obesity. Subjects with high-normal FPG show a worse cardiometabolic profile than those with low-normal FPG. Although our observations need to be confirmed in the general pediatric population, the simple measurement of FPG may help in identifying children who warrant some monitoring. Longitudinal studies will confirm whether high-normal FPG in childhood could be considered a marker of cardiovascular risk and a predictor of hard outcomes in adulthood.

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P.D.B. had the original idea and wrote the manuscript. E.S., C.F., and F.S. collected clinical data. M.R.I. performed biochemical assays. B.C. reviewed and edited the manuscript.

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**Table 1—Anthropometric, clinical, and biochemical variables among categories of FPG and risk of CMRF in children and adolescents**

| Categories of FPG | Low (n=274) | Mid (n=275) | High (n=231) | P |
|------------------|------------|------------|-------------|---|
| n                | 274        | 275        | 231         |   |
| Age (years)      | 10 ± 3     | 10 ± 3     | 10 ± 3      | 0.101 |
| Boys (%)         | 110 (40%)  | 143 (52%)  | 129 (56%)   | 0.001 |
| Prepubertal stage (%) | 135 (49%) | 145 (53%) | 112 (49%) | 0.586 |
| Normal weight (%)| 92 (33%)   | 61 (22%)   | 45 (20%)    | 0.0001 |
| Overweight (%)   | 62 (23%)   | 59 (21%)   | 53 (23%)    | 0.554 |
| Obesity (%)      | 120 (44%)  | 155 (56%)  | 133 (58%)   | 0.001 |
| BMI (kg/m²)      | 24 ± 6     | 25 ± 6     | 26 ± 6      | 0.0001 |
| BMI z score      | −0.22 ± 1.0| 0.02 ± 0.96| 0.19 ± 1.02 | 0.0001 |
| Waist circumference (cm) | 77 ± 17 | 82 ± 16 | 85 ± 17 | 0.0001 |
| HOMA-IR          | 1.9 ± 1.4  | 2.7 ± 2.1  | 3.4 ± 2.5   | 0.0001 |
| HbA1c (%)        | 5.4 ± 0.3  | 5.4 ± 0.3  | 5.3 ± 0.3   | 0.118 |
| Cholesterol (mg/dL) | 162 ± 33  | 163 ± 30   | 161 ± 32   | 0.792 |
| HDL cholesterol (mg/dL) | 52 ± 11  | 53 ± 11    | 52 ± 12   | 0.264 |
| Triglycerides (mg/dL) | 84 ± 40  | 87 ± 44    | 84 ± 36   | 0.902 |
| BP (mmHg)        |           |           |            |   |
| Systolic         | 103 ± 11   | 107 ± 12   | 110 ± 13   | 0.0001 |
| Diastolic        | 60 ± 9     | 60 ± 10    | 61 ± 9     | 0.542 |
| WBC (10^3/L)     | 7.1 ± 2.4  | 7.4 ± 2.0  | 7.9 ± 2.3  | 0.0001 |
| Odds ratio (95% CI)^ |       |           |            |   |
| Insulin resistance| 1.00      | 2.35 (1.43–3.87)* | 1.95 (1.52–2.51)† |   |
| Hypertension     | 1.00       | 2.23 (1.06–4.08)§ | 1.57 (1.07–2.29)¶ |   |
| High WBC count   | 1.00       | 1.00 (0.63–1.38)* | 1.31 (1.05–1.65)* |   |

Data are mean ± SD or n (%) unless otherwise indicated. *Adjusted for age, sex, pubertal stage, allergy, and BMI z score; †P < 0.001; §P < 0.0001; ¶P < 0.05; ‡P < 0.025.
Glucose and cardiometabolic risk factors

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