Prevention of Type II Diabetes by Physical Training

Epidemiological considerations and study methods

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Disease prevention may be considered at three levels: primary (avoiding disease occurrence), secondary (early detection and reversal), and tertiary (prevention or delay of complications). Physical exercise could potentially contribute to all of these. Metabolic studies suggest the major effect of exercise is at the level of insulin sensitivity/resistance. Therefore, it may have the greatest benefit in primary prevention and in the early stages of the disease. Studies of migrants and of active and inactive professions support this notion. There is also provisional support for the benefit of exercise on metabolic control and prevention or delay of chronic complications in non-insulin-dependent (type II) diabetic patients. In designing a trial of exercise, aspects such as single/multifactorial intervention, the age range of subjects, and choice of outcome measures must be considered. The most widely used methodological tool in assessing physical activity levels in population studies is the activity questionnaire, which is nonreactive, practical, applicable, and accurate relative to other methods. A positive approach to exercise training for both the patient with type II diabetes and the general community appears to be warranted. However, trials examining the efficacy of activity intervention, with independent evaluation of both short- and long-term outcomes, are still needed.

It is the role of epidemiology not only to assess the distribution and determinants of disease in human populations, but also to apply the results of such study to the control of health problems in whole communities (1). Thus, epidemiology is not merely an academic discipline. As the practical science of public health, it has an important contribution to make to research in the field of disease prevention.

Disease prevention may be considered in three broad areas. *Primary prevention* implies averting the occurrence of ill health in susceptible persons or communities. Strategies include both population-based and high-risk approaches, and various mixtures of the two (2–7).

Secondary prevention implies the early detection and reversal of ill health before adverse complications arise. In the knowledge that primary prevention, however desirable, is very difficult to achieve in practice, secondary prevention of diabetes is a subject of increasing interest. As with primary prevention, both population approaches (mass screening) and high-risk strategies (selective screening) can be considered (8).

Tertiary prevention is concerned with the prevention or delay of complications in ongoing and established cases of disease. Because it is not so much the functional state of glucose intolerance—but its adverse cardiovascular, renal, neurological, and other effects that are of such consequence in diabetes—tertiary prevention takes on a special importance in this disease.

EVIDENCE FOR AN ASSOCIATION BETWEEN DIABETES AND EXERCISE

The strength and importance of the relationship between physical activity and non-insulin-dependent (type II) diabetes are likely to vary across the spectrum of glucose tolerance (from normal tolerance through impaired tolerance to overt diabetes). Although the primary abnormality in type II diabetes is still a subject for debate, findings from the Pima Indian studies (9) suggest that insulin resistance appears to predominate early in the course of glucose intolerance, with insulin deficiency developing later. Metabolic studies have demonstrated that the major effect of physical activity is in terms of insulin sensitivity/resistance (10). Therefore, one could anticipate that physical activity might have the greatest influence on the progression of the disease in the early stages of intolerance when insulin resistance is the major cause for the abnormal glucose response. By extrapolation, one might expect that physical activity would be more effective in preventing deterioration from normal tolerance than in reversing existing intolerance.

Primary prevention

In addition to demonstrating that the relationship between physical activity and

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type II diabetes is biologically plausible, the previously stated argument suggests a role for exercise, especially in primary prevention. It has been suggested that physical activity could decrease the occurrence of type II diabetes either directly (by increasing insulin sensitivity) or indirectly (by preventing obesity and/or beneficially altering the distribution of fat) (11).

Many societies that have recently abandoned traditional life-styles have experienced a major increase in incidence of type II diabetes. In most cases, sociocultural change has been associated closely with the adoption of sedentary living and markedly reduced habitual physical exercise (12).

Migrant studies provide further support for this notion. Kawate et al. (13) compared Japanese living in Hiroshima with those who had migrated to Hawaii. Despite similar genetic backgrounds, prevalence of diabetes was almost twice as high in the Hawaiian group, and this association was independent of age, gender, and obesity. Classifying individuals in terms of occupational activity, a larger proportion of the nonmigrants engaged in heavy work, suggesting that this factor might have a protective effect.

Studies of the consequences of habitation in a rural versus an urban environment have also provided indirect evidence of a potentially protective effect of physical activity. Rural-urban comparison of residents of Puerto Rico (14) and several Pacific islands, including Western Samoa (15), Fiji (16), and Kiribati (17), all demonstrated increased risk in the urban dwellers that could not be explained by obesity alone. In Fiji, diabetes was found to be more prevalent in inactive subjects than in habitually active individuals (18), although a wider examination of Pacific data found this relationship to be inconsistent (19).

Plasma glucose and insulin values were found to be higher in office workers than in physical laborers in a study of nondiabetic Taiwanese males (20). In studies of nondiabetic participants from a community health screening program, postglucose load values for blood glucose (21,22) and insulin (21) were significantly lower in those males who reported relatively higher levels of leisure-time activity (based on questionnaire responses) than those reporting little activity. Other studies of similar design, in which males were classified according to self-reported activity, demonstrated similar although nonsignificant trends, with least active subjects having the poorest glucose tolerance (23), or found no relationship between activity and glucose tolerance at all (24).

Taken as a whole, the evidence does suggest that physical activity and glucose tolerance seem to be related. What remains uncertain from these cross-sectional studies is whether physical inactivity is the cause or the effect of the glucose intolerant state. In addition, the degree to which the beneficial effect of activity may be mediated through prevention of obesity or through a decrease in centrally distributed obesity is not yet known.

The results of one (historical) prospective study are also somewhat encouraging. In most age-groups, a lower incidence of diabetes was observed in female college alumni who were former athletes than in those who were not (25). However, a higher proportion of the former athletes also reported regular exercise at the time of the investigation, so that the effects of historical and contemporary activity on glucose tolerance status could not be separated. Furthermore, in this study, the diagnosis of diabetes was based on self-report.

Further prospective research is required before the relationship between physical inactivity, obesity, and the development of type II diabetes can be fully understood. Meanwhile, physical activity is being encouraged on a community basis in the primary prevention of several chronic diseases, especially coronary heart disease and its associated conditions (26,27). To date, there have been no primary prevention projects for type II diabetes that have utilized physical activity as the sole intervention.

Secondary and tertiary prevention

Clinical studies investigating the effect of an acute bout of exercise in type II diabetic individuals generally demonstrate a beneficial lowering of plasma glucose levels (28). The effect of chronic activity or exercise training for type II diabetic subjects is still being debated. Different outcomes reported in various exercise training studies may be caused by differences in disease progression among the participants. It appears that those who have received the greatest benefit from physical training are subjects with relatively mild disease (29,30).

As an example, the beneficial effect of 7 days of exercise in 10 men with mildly abnormal glucose tolerance (31) is illustrated in Fig. 1. These findings entirely agree with the notion that physical activity is most useful, in terms of improving insulin sensitivity, early in the disease, when B-cell function may still be relatively intact.

In addition to the results of these clinical studies, findings from two community-based studies have suggested a beneficial effect of physical activity for subjects with type II diabetes. In 1983, an exercise program was initiated among the Zuni Indians, who have a very high prevalence of type II diabetes (32). Over a 2-yr period, comparing 30 diabetic exercise participants with 56 diabetic nonparticipants, the participants lost more weight, had a greater drop in fasting blood glucose concentration, and were more likely to have decreased or stopped medication (Fig. 2).

Analogous to the results of the Zuni project are those of a trial of exercise combined with reversion to a traditional diet in diabetic Australian Aborigines. O'Dea (33) took a small number of volunteers into a desert setting for 7 wk, in a deliberate attempt to recreate the ancestral environment. Carbohydrate metabolism improved significantly, and

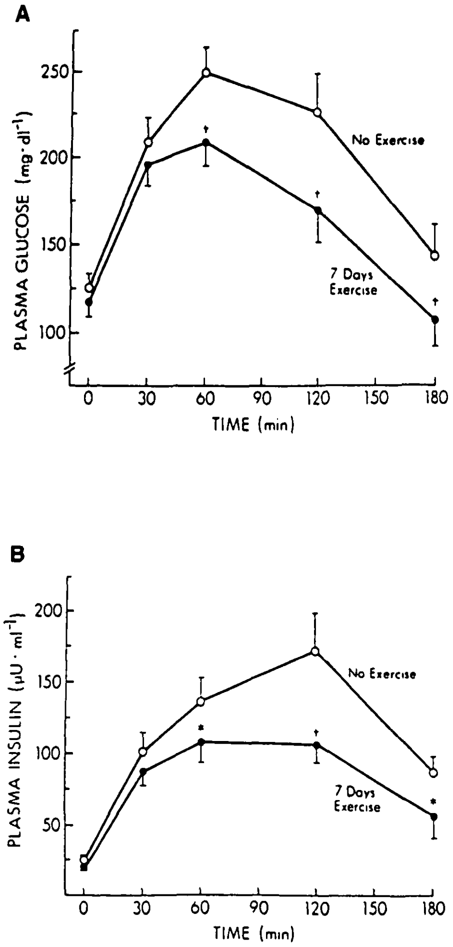

Figure 1—*Effect of 7 days exercise on plasma glucose (A) and insulin (B) responses to 100-g oral glucose tolerance test. Means ± SE for 10 subjects. From Rogers et al. (30). © by the American Diabetes Association.*

this was attributed to changes in weight, composition of the diet, and exercise.

A limitation of both of these studies was the nonrandom allocation of subjects because participants were self-selected. More recently, a clinical study demonstrated that physical activity and dietary treatment can result in enhanced glycemic control and long-term weight loss in the type II diabetic individual (34).

In summary, these few reports do suggest that motivated subjects with type II diabetes can benefit from an exercise program, providing encouragement for the advocates of this approach to secondary and tertiary prevention of the disease. The potential benefits of physical exercise for the type II diabetic patient have been summarized in a position statement by the American Diabetes Association (35).

DEVELOPING A TRIAL OF EXERCISE IN THE PREVENTION OF TYPE II DIABETES— In designing a physical activity intervention trial, many factors must be kept in mind. There are certain choices to be made with respect to the study design that will effect the outcome and interpretation of the trial.

At the outset, it is necessary to decide whether the trial should be restricted to a single factor (in this case, physical activity intervention) or whether a wider intervention aimed at several potential risk factors (diet, obesity) is to be preferred. To some extent, this choice should be guided by knowledge of the risk factor profile in the target community (5).

Concerning the choice of subjects to enter the trial, one important consideration is age criteria. Because type II diabe-

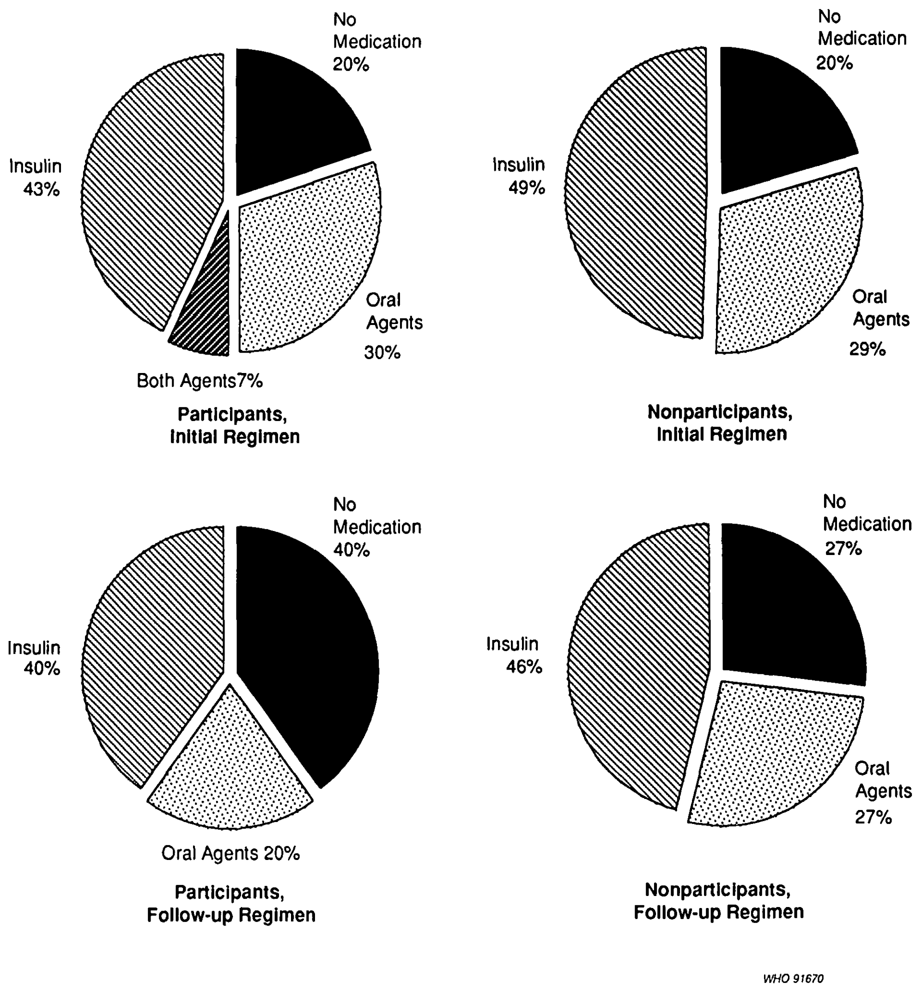

Figure 2—*Medication status for participants and nonparticipants in the Zuni Diabetes Project. Comparison of initial and follow-up regimens. From Heath et al. (32). © by the American Diabetes Association.*

tes is strongly age dependent, it might be more efficient to study the age range at which the onset of the disease is most common. However, if the disease were thought to have a long prodrome and early influences were considered important, a long trial including subjects of younger ages would need to be contemplated. Interest in early or late stages of the disease would be a further consideration.

Depending on whether interest centers on high-risk or fully population-based strategies, the trial could either be limited to subjects demonstrating known risk factors, or could recruit subjects from the community without regard to their estimated risk. Choice of outcome measures will have an important bearing on the study design. Ideally, the measure of effect should be change in disease incidence for primary prevention measures, or change in incidence of complications and mortality for tertiary prevention measures. For measures aimed at secondary prevention, reversal of glucose intolerance should be a suitable endpoint. A trial of more limited scope might choose reduction of modifiable risk factors as an end point, enabling a faster result and a smaller number of subjects to be involved (before/after comparisons of continuously distributed variables have much greater power than those comparing disease status, especially if the condition is rare).

Many of these decisions will have an influence on the extrapolation of the findings of the trial. A restrictive design may have high internal validity, but not be readily generalized, whereas a broadly based trial may have greater external validity, but may not produce results with the same degree of specificity and precision.

ASSESSMENT OF PHYSICAL ACTIVITY IN EPIDEMIOLOGICAL STUDIES — The physical activity questionnaire is currently the most widely used method for the assessment of physical activity in population studies (36,37). Reasons for its popularity include its nonreactiveness (lack of alteration of the individual's behaviors as a direct result of the assessment technique), its practicality (generally determined by cost and participant convenience), its applicability (ability to modify the instrument to suit the population in question), and its accuracy (both reliability and validity) relative to other methods. In contrast, more objective measures of energy expenditure, such as activity monitors and the doubly labeled water technique, are not practical for use on a population level, but may be used to validate specific components of the physical activity questionnaire.

Despite differences in their time frame, focus, and presentation, many of the popular questionnaires have been found to be reasonably accurate and to correlate significantly with physiological variables thought to be associated with physical activity. Presented in a comprehensive review by Washburn and Montoye (38), most of these questionnaires were used in coronary heart disease research. More recently, a thorough discussion of the rationale, design, and evaluation of a physical activity questionnaire that was specifically developed to examine the relationship between physical activity and type II diabetes in the Pima Indian Study has been published (39).

EVALUATION OF AN INTERVENTION TRIAL — Any scientific trial should include a careful evaluation of the results. This should not only consider beneficial effects, but also potential negative outcomes and risks (injury, for example, in the case of physical training). Both financial and opportunity costs need to be considered in light of the observed effects in order to estimate cost/benefit, which should include quality of life and financial parameters.

When considering the efficacy of prevention, one must consider not only the pragmatic question (can it work?), which may be determined by biochemical and/or physiological factors, but also the empirical question (will it work?), which is also influenced by social, cultural, and practical considerations. Given the need to influence voluntary behavior in most chronic disease prevention trials, acceptability to the target population, not only on the short term but also more permanently, may often be the greatest determinant of outcome.

It has been shown that postintervention compliance to life-style activity is better than high-intensity aerobic programs (40). In general, activities with greater intensities are associated with poorer compliance. It is therefore important that both short- and long-term compliance be included in any formal evaluation of outcome.

CONCLUSIONS — Preventive measures may be divided into those that seek to impose new habits and activities, and those that seek to restore formerly beneficial ones that a community may have abandoned. Generally, new and "unnatural" interventions (such as drug therapy) should not be recommended without clear evidence of their efficacy. On the other hand, to restore biological normality may be advocated with less reservation (41).

Because physical exercise was a natural component of the life-style of most cultures before industrialization and the accompanying urban drift, its adoption now could be considered a return to greater biological normality. This consideration, combined with the limited clinical and epidemiological evidence presented, seems to warrant a positive approach to exercise training at the level of both the patient with type II diabetes (in terms of secondary and tertiary prevention) and the community as a whole (with a view to primary prevention, most likely as a part of a broader, healthy life-style initiative). However, there is a continuing need for formal trials of efficacy, with independent evaluation of both short- and long-term outcomes.

References

1. Last JM: *A Dictionary of Epidemiology*. New York, Oxford University Press, 1983
2. World Health Organization: *From Alma-Ata to the Year 2000. Reflections at the Midpoint*. Geneva, World Health Organization, 1988
3. Tuomilehto J, Wolf E: Primary prevention of diabetes mellitus. *Diabetes Care* 10:238–48, 1987
4. Zimmet PZ: Primary prevention of diabetes mellitus. *Diabetes Care* 11:258–62, 1988
5. King H, Dowd JE: Primary prevention of type 2 (non-insulin-dependent) diabetes mellitus. *Diabetologia* 33:3–8, 1990
6. Epstein FH, Holland WW: Prevention of chronic diseases in the community—one-disease versus multiple-diseases strategies. *Int J Epidemiol* 12:135–37, 1983
7. Glasunov IS, Grabauskas V, Holland WW, Epstein FH: An integrated programme for the prevention and control of noncommunicable diseases. *J Chron Dis* 36:419–26, 1983
8. American Diabetes Association: Position statement: screening for diabetes. *Diabetes Care* 12:588–90, 1989
9. Lillioja S, Mott DM, Howard BV, Bennett PH, Yki-Jarvinen H, Freymond D, Nyomba BL, Zurlo F, Swinburn B, Bogardus C: Impaired glucose tolerance as a disorder of insulin action. *N Engl J Med* 318: 1217–25, 1988
10. Koivisto VA, Yki-Jarvinen H, DeFronzo RA: Physical training and insulin sensitivity. *Diabetes Metab Rev* 1:445–81, 1986
11. Despres JP, Tremblay A, Nadeau A, Bouchard C: Physical training and changes in regional adipose tissue distribution. *Acta Med Scand* 723 (Suppl.):205–12, 1988
12. Zimmet P, Dowse G, Finch C, Serjeantson S, King H: The epidemiology and natural history of NIDDM—lessons from the South Pacific. *Diabetes Metab Rev* 6:91–124, 1990
13. Kawate R, Yamakido M, Nishimoto Y, Bennett PH, Hamman RF, Knowler WC: Diabetes and its vascular complications in Japanese migrants on the island of Hawaii. *Diabetes Care* 2:161–70, 1979
14. Cruz-Vidal M, Costas R, Garcia-Palmieri M, Sorlie P, Hertzmark E: Factors related to diabetes in Puerto Rican men. *Diabetes* 28:300–307, 1979
15. Zimmet P, Faaiuso S, Ainuu S, Whitehouse S, Milne B, DeBoer W: The prevalence of diabetes in the rural and urban Polynesian population of Western Samoa. *Diabetes* 30:45–51, 1981
16. Zimmet P, Taylor R, Ram P, King H, Sloman G, Raper LR, Hunt D: The prevalence of diabetes and impaired glucose tolerance in the biracial (Melanesian and Indian) population of Fiji: a rural-urban comparison. *Am J Epidemiol* 118:673–88, 1983
17. King H, Taylor R, Zimmet P, Pargeter K, Raper LR, Beriki T, Tekanene J: Non-insulin-dependent diabetes (NIDDM) in a newly independent Pacific nation—the Republic of Kiribati. *Diabetes Care* 7:409–15, 1984
18. Taylor R, Ram P, Zimmet P, Raper LR, Ringrose H: Physical activity and prevalence of diabetes in Melanesian and Indian men in Fiji. *Diabetologia* 27:578–82, 1984
19. King H, Zimmet P, Raper LR, Balkau B: Risk factors for diabetes in three Pacific populations. *Am J Epidemiol* 119:396–409, 1984
20. Wang JT, Ho LT, Tang KT, Wang LM, Chen YDI, Reaven GM: Effect of habitual physical activity on age-related glucose intolerance. *J Am Geriatr Soc* 37:203–209, 1989
21. Lindgarde F, Saltin B: Daily physical activity, work capacity and glucose tolerance in lean and obese normoglycaemic middle-aged men. *Diabetologia* 20:134–38, 1981
22. Cederholm J, Wibell L: Glucose tolerance and physical activity in a health survey of middle-aged subjects. *Acta Med Scand* 217:373–78, 1985
23. Montoye HJ, Block WD, Metzner H, Keller JB: Habitual physical activity and glucose tolerance: Males aged 16–64 in a total community. *Diabetes* 26:172–76, 1977
24. Jarrett RJ, Shipley MJ, Hunt R: Physical activity, glucose tolerance and diabetes mellitus: the Whitehall study. *Diabetic Med* 3:549–51, 1987
25. Frisch RE, Wyshak G, Albright TE, Albright NL, Schiff I: Lower prevalence of diabetes in female former college athletes compared with nonathletes. *Diabetes* 35: 1101–1105, 1986
26. Harris SS, Caspersen CJ, DeFriese GH, Estes EH: Physical activity counseling for healthy adults as a primary preventive intervention in the clinical setting: Report for the US Preventive Services Task Force. *JAMA* 261:3588–98, 1989
27. Committee on Health Promotion, Faculty of Community Medicine of the Royal Colleges of Physicians of the United Kingdom: Guidelines for health promotion no. 7. Promoting exercise in the community (no date).
28. Minuk HL, Vranic M, Marliss EB, Hanna AK, Albisser AM, Zinman B: Glucoregulatory and metabolic response to exercise in obese non-insulin-dependent diabetes. *Am J Physiol* 240:E458–64, 1981
29. Holloszy JO, Schultz J, Kusnierkierkiewicz J, Hagberg JM, Ehsani AA: Effects of exercise on glucose tolerance and insulin resistance. *Acta Med Scand* 711 (Suppl.):55–65, 1986
30. Schneider SH, Amorosa LF, Khachadurian AK, Ruderman NB: Studies on the mechanism of improved glucose control during regular exercise in type 2 diabetes. *Diabetologia* 26:355–60, 1984
31. Rogers MA, Yamamoto C, King DS, Hagberg JM, Ehsani AA, Holloszy JO: Improvement in glucose tolerance after 1 week of exercise in patients with mild NIDDM. *Diabetes Care* 11:613–18, 1988
32. Heath GW, Leonard BE, Wilson RH, Kendrick JS, Powell KE: Community-based exercise intervention: Zuni diabetes project. *Diabetes Care* 10:579–83, 1987
33. O'Dea K: Marked improvement in carbohydrate and lipid metabolism in diabetic Australian Aborigines after temporary reversion to traditional lifestyle. *Diabetes* 33:596–603, 1984
34. Wing RR, Epstein LH, Bayles MP, Kriska AM, Nowalk MP, Gooding W: Exercise in a behavioural weight control programme for obese patients with type 2 (non-insulin-dependent) diabetes. *Diabetologia* 31:902–909, 1988

35. American Diabetes Association Council on Exercise: Position statement: diabetes mellitus and exercise. *Diabetes Care* 13: 804–805, 1990
36. Montoye HJ, Taylor HL: Measurement of physical activity in population studies: a review. *Hum Biol* 56:195–216, 1984
37. LaPorte RE, Montoye HJ, Caspersen CJ: Assessment of physical activity in epidemiologic research: problems and prospects. *Public Health Rept* 100:131–46, 1985
38. Washburn RA, Montoye HJ: The assessment of physical activity by questionnaire. *Am J Epidemiol* 123:563–76, 1986
39. Kriska AM, Knowler WC, LaPorte RE, Drash AL, Wing RR, Blair SN, Bennett PH, Kuller LH: Development of questionnaire to examine the relationship of physical activity and diabetes in the Pima Indians. *Diabetes Care* 13:401–11, 1990
40. Epstein LH, Wing RR, Koeske R, Valoski A: A comparison of lifestyle exercise, aerobic exercise, and calisthenics on weight loss on obese children. *Behaviour Therapy* 16:345–56, 1985
41. Rose G: Sick individuals and sick populations. *Int J Epidemiol* 14:32–38, 1985