

Primary Prevention of Diabetes Mellitus

Two-thirds of all deaths in developed countries are caused by the major noncommunicable diseases, e.g., cardiovascular disease, cancer, and non-insulin-dependent diabetes mellitus (NIDDM). There is increasing evidence that these diseases are a consequence of life-style change, and they have a number of risk factors in common. Primary prevention of both insulin-dependent diabetes mellitus (IDDM) and NIDDM has become increasingly important because of their significant morbidity and mortality and the human and economic costs associated with diabetes and its complications. Prevention of the two major forms of diabetes, IDDM and NIDDM, are quite separate issues. The former appears to be an autoimmune disorder, whereas the latter should be considered along with other life-style-related noncommunicable diseases. The primary prevention of NIDDM appears to offer the greatest promise of success. The uncertainty that still exists as to the role of obesity and other risk factors in the development of NIDDM gives support to a multiple-risk-factor intervention approach (through a healthy life-style strategy) for NIDDM prevention. *Diabetes Care* 11:258-62, 1988

In developed countries the major noncommunicable diseases (NCDs), e.g., cardiovascular disease (CVD), cancer, and non-insulin-dependent diabetes mellitus (NIDDM), are responsible for over two-thirds of all deaths (1). There is increasing evidence that these diseases are a consequence of life-style (2). In fact, with industrialization and modernization of life-style in

many developing countries, NCDs are rapidly overtaking communicable diseases as the major causes of death.

The foundations of modern epidemiology were laid in the nineteenth century when studies on epidemics of yellow fever and cholera resulted in their successful control. Such early successes set the pace for community-oriented public-health measures.

It is paradoxical that the control of communicable diseases has partly resulted in the escalation of NCD, because this control, along with other measures for improved public health, has led to longer life expectancy. Earlier in this century, life expectancy in many societies was such that most people did not live long enough to develop NIDDM, hypertension, and CVD.

The two major forms of diabetes, insulin-dependent diabetes mellitus (IDDM) and NIDDM, need to be considered separately, both in an etiological and a preventive perspective. Prevention of IDDM is a separate issue from prevention of NIDDM, which should be considered along with other NCDs. The prevention of NIDDM appears to offer the greatest promise of success.

In general, prevention of both forms of diabetes has become increasingly important in view of the increased morbidity and mortality due to diabetes in both developed and developing countries and the socioeconomic costs associated with diabetes and its complications (3). Secondary and tertiary prevention with respect to diabetes are well-accepted strategies already, and we therefore focus on primary prevention.

STRATEGIES FOR PRIMARY PREVENTION

Primary prevention is aimed at reducing the incidence of disease and other departures from good health. What is actually meant by primary prevention? Primary pre-

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vention, in the context of NCD, can be defined as the promotion of health by personal and communitywide efforts, e.g., improving nutritional status, physical fitness, and emotional well-being (4).

Guidelines for a comprehensive plan for primary prevention of coronary heart disease have been published by the World Health Organization (WHO) (5). More recently, WHO has provided guidelines for community prevention and control of CVDs (6). These guidelines, applicable to NIDDM, include two components: 1) a population strategy for altering the life-style and environmental characteristics and their social and economic determinants that are the underlying causes of NIDDM, and 2) a high-risk strategy for bringing preventive care to individuals at special risk.

In many areas of the world, including a few developed countries, life-styles have not yet acquired the pattern associated with a high NIDDM incidence, and the average level of major risk factors is still favorable. Socioeconomic life-style changes threaten to undermine this situation. In such circumstances, it becomes urgent to consider primordial prevention, i.e., preventing the emergence of predisposing risk factors in countries in which they have not yet appeared (5).

PREVENTION OF NON-INSULIN-DEPENDENT DIABETES MELLITUS

As mentioned earlier, the major communicable diseases were eliminated or controlled in developed countries in the early part of this century. This process is now occurring in the developing world. People are living longer, but their behavior and their environment have changed, resulting in overnutrition, less physical activity, and greater stress. Simultaneously, the incidence and prevalence of NCDs—CVD, hypertension, and cancer as well as NIDDM—have risen in many developing nations (1,7).

Potential for prevention. Sufficient data have accumulated to initiate community-based prevention programs for NIDDM (8). The disease appears to be linked with sedentary living, overnutrition, and obesity, and attention to these factors may reduce the incidence, prevalence, and complications of NIDDM (9). However, because little can be done to change genetic susceptibility, prevention programs may need to be directed at reducing the level of risk factors in high-risk individuals or whole populations.

The familial nature of NIDDM at least allows the identification of high-risk individuals and the direction of specific prevention strategies toward such individuals (10). Although no genetic marker for NIDDM has been discovered, the rapid advances in molecular genetics provide hope that the location of the gene(s) that may be important in defining susceptibility may soon be found. This discovery could provide the ability to better define the individuals at high risk of developing NIDDM.

Reversion of environmental risk factors probably ex-

plains the dramatic fall in CVD mortality in some industrialized nations, e.g., the United States, Finland, Belgium, and Australia (1). It is appropriate to establish whether NIDDM can also be prevented in a similar manner.

Rationale for prevention. Increasing morbidity and mortality from diabetes in developing populations has resulted in escalating costs due to medical care, disability, and premature mortality (3). This cost provides a major incentive for the initiation of effective prevention programs.

Key activities in the planning of any diabetes prevention program are to define the environmental and behavioral risk factors for NIDDM in the population. The striking emergence of NIDDM as a major health problem in populations undergoing modernization of life-style strongly suggests the importance of environmental factors (11). The fact that NIDDM is either absent or rare in traditional-living communities suggests that factors resulting from acculturation may be of major importance. However, the major problem is to ascertain which factor or combination of factors is operative. This is difficult because many environmental and behavioral changes are likely to occur simultaneously with the process of modernization of way of life.

The development of prevention programs for diabetes in any community depends on accurate data on behavioral and environmental risk factors for the disease. In certain populations, a strong association has been demonstrated between obesity and NIDDM (11,12). Thus, programs aimed at reducing the level of obesity may reduce the incidence and prevalence of NIDDM. However, it is pointless to concentrate on control and prevention of obesity when it has not been shown to be the sole, or a major, risk factor in a community.

New evidence has emerged from at least two population studies that obesity is not the only, and may not be the most important, risk factor for NIDDM (13,14). The first of these studies suggests heterogeneity for risk factors in NIDDM between people within the same ethnic group and between populations of different ethnic backgrounds, including such factors as physical inactivity and composition of the diet (13).

No report exists of a population study in which reduction of obesity has prevented the development of diabetes. If obesity is shown to be the key (or a major) factor in causing diabetes in populations with high NIDDM prevalence, as seen in Pima Indians (15), Nauruans (16), or Maltese (17), then these would be important groups in which to target such an intervention. Because uncertainty still exists as to the role of obesity in the etiology of NIDDM, multiple-risk-factor intervention would be a logical approach toward NIDDM prevention (8).

Just as the role of obesity as a risk factor is controversial, so are the roles of diet and stress. Although additional data are clearly required, extensive studies have not revealed a significant relationship between the composition of the diet (complex vs. refined carbohydrates, fiber, fat, or protein) and NIDDM, although

caloric excess (possibly mediated through obesity) may be of etiologic significance (11,18).

An improvement in glucose tolerance has been noted after exercise training in people with NIDDM (19). If sedentary life-style is shown to be an etiological factor for NIDDM in any community, a controlled study should be undertaken to assess the role of promoting exercise as an intervention in NIDDM prevention. Frisch et al. (20) found a lower prevalence of diabetes in female former college athletes (0.57%) compared with nonathletic classmates (1.3%) and concluded that long-term athletic training is associated with a lower risk of the development of diabetes. Furthermore, epidemiological studies in Pacific populations have shown lower diabetes prevalence in physically active male subjects (21).

Temporary reversion to traditional life-style has been shown to greatly improve or completely normalize the major metabolic abnormalities of NIDDM in a group of Australian Aborigines (22). The high prevalence of NIDDM has been well documented in urbanized Australian Aborigines, and diabetes now represents a serious public-health problem in this community, a situation evident in several ethnic groups, including Polynesians and Micronesians, American Indians, migrant Asian Indians, and Mexican Americans (10,11). These are populations that have changed from a more traditional to a more modern way of life.

The major finding of the Australian Aboriginal study was the marked improvement in glucose tolerance in 10 diabetic subjects after a 7-wk return to their traditional hunter-gatherer life-style (22). There was improvement of both insulin secretion and insulin action, two of the major metabolic defects in NIDDM, in parallel with the life-style change. At least three factors known to improve insulin sensitivity were operating in this study—weight loss, low-fat diet, and increased physical activity. Similar results have been achieved in Pima Indians with NIDDM who were placed on a hy-

pocaloric diet (23). Thus, the incorporation of healthy life-style changes into a prevention program might result in the prevention of NIDDM in larger population-based studies.

Implementation of prevention program. There is evidence for heterogeneity of environmental risk factors for NIDDM between sexes within a given population and between populations (13). Therefore, before embarking on a community prevention program, it is essential that a careful epidemiological survey be carried out to determine the risk factors for NIDDM in that population. The basic steps for development of a prevention program are shown in Fig. 1.

Before an intervention program is begun, a full community assessment that includes knowledge of the relevant risk factors for NIDDM and data on prevalence, incidence, morbidity, and mortality is essential. An assessment of community attitudes on the various interventions proposed should be carried out, and political agreement on strategies should be sought.

After analysis of these data and discussion with appropriate authorities and community representatives, the intervention strategy can be planned. Once there is agreement at the appropriate levels (national, regional, and community), the intervention program can be implemented. A critical component of the program will be the evaluation of its impact on the target community.

The prevention of NIDDM will involve action by all sectors of the community—government, media, education, and health services—as well as the general population. Prevention programs will need to be integrated into existing health services, including the primary health-care system, and into existing prevention programs (e.g., those already in place for prevention of CVD and/or hypertension). Such an approach is consistent with the recommendations of WHO with respect to an integrated approach to prevention and control of NCDs (3). Not only is this approach logical, it is also cost-effective, particularly in developing countries (6,8).

PREVENTION OF INSULIN-DEPENDENT DIABETES MELLITUS

A better understanding of genetic markers and the genetics of IDDM is of more than academic interest because of interest in possible prevention of IDDM by immune intervention (24). However, for this to be feasible, definition of subjects at high risk is required, and histocompatibility leukocyte antigen (HLA) typing of entire communities is not feasible or economic. Apart from this, at least 50% of Caucasians are HLA-DR3/DR4 (25,26), but only ~0.2% of the population actually develop IDDM.

Several immunological abnormalities, including the presence of islet cell antibodies, can be demonstrated several years before the acute onset of IDDM (24). However, for the purpose of genetic screening and counseling and for prevention, HLA-DR typing would only be

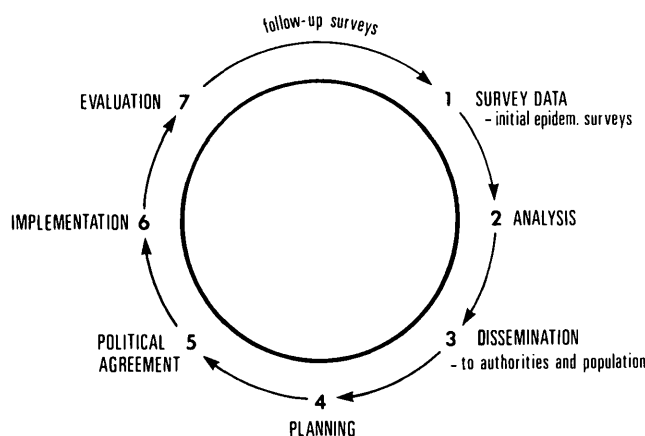


FIG. 1. Strategy for development and implementation of prevention program for noncommunicable diseases, including non-insulin-dependent diabetes.

feasible in families where at least one child or parent has IDDM. In this situation, HLA typing allows identification of first-degree relatives at risk of developing IDDM. The cost of screening the whole population would far outweigh the potential benefit.

Until the degree of susceptibility of an individual can be determined with greater precision and more effective means are available to slow or arrest the pathogenic process, a specific high-risk strategy cannot be recommended. However, advances in knowledge make it important to keep this question under review.

Recently, a form of prevention called *postprimary* has been attempted. The basis of this form of prevention is to arrest the pathogenic process of autoimmune β -cell destruction (24). There is strong presumptive evidence that in genetically predisposed individuals, self-damaging immunological mechanisms are involved in development of IDDM. These are triggered by unidentified environmental agents, and effective primary prevention awaits their identification. As a form of postprimary prevention, several centers are undertaking studies of the effect of immune suppression via cyclosporin in new cases of IDDM (24). However, primary prevention of IDDM does not yet seem appropriate.

CONCLUSIONS

The major causes of morbidity and mortality in adults in developed countries appear to be the result of life-style (2,3,5–8). CVD, obesity, hypertension, and NIDDM provide excellent examples of this phenomenon. Although there may be a clear relationship, the epidemiological and other scientific evidence and possible mechanisms contain numerous gaps (8). As a result, it could be argued that, particularly in the case of NIDDM, uncertainty exists as to whether large-scale population prevention programs can be justified on the basis of existing data.

We must weigh the benefits, risks, and costs of such interventions. In addition, the hasty development of a multiple-risk-factor intervention study may not advance our knowledge of causal factors or which of the multiple interventions might be central and critical and which are secondary.

Because a further 10–20 yr of prospective studies may be necessary to accumulate the appropriate data, those responsible for improving public health are faced with a major and historic decision. The success of CVD and hypertension prevention programs in numerous countries suggests that changes in life-style are effective for NCD prevention (5–8,27,28). How much more evidence do we need before we take action on the escalating problem of NIDDM and its associated morbidity and mortality? Can any harm come from recommending a healthy life-style in an attempt to prevent NIDDM?

Epstein (29) has stated the case for NCD prevention in the clearest possible terms: "Ultimate 'proof' that prevention works will probably never be obtained but the

evidence at hand justifies the pragmatic approach to go ahead with putting into action what has been learned. To keep looking on while, so to speak, Rome burns is not defensible anymore."

Little harm can come from national programs stressing the importance of a healthy life-style—good nutrition, avoidance of obesity, increased physical activity, reduction in smoking and alcohol consumption, and avoidance of stress—providing they do not cause insensitive interference with local customs and values in the target community. These strategies can be seen as interim measures while the results of long-term epidemiological studies and their evaluation are awaited.

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