The Diabetes Epidemic: Description of the Problem
The Diabetes Epidemic: Genes and Environment Clashing

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Introduction

Diabetes mellitus affects large numbers of people from a wide range of ethnic groups and at all social and economic levels throughout the world.\(^1\) The last few decades of the 20th century saw an explosive increase in this disorder globally, mainly in the number of people with Type 2 diabetes. At the present time it is estimated that 190 million people worldwide have diabetes and that this will increase to 324 million by 2025.\(^2\) The epidemic is taking place in both developed and developing nations.

Over the last 40 years, there have been dramatic changes in the human environment, behaviour and lifestyle. These changes have resulted in escalating rates of both obesity and diabetes.\(^3\) There is every reason to believe that over the next decade the epidemic of Type 2 diabetes will continue to escalate. It is for this reason that the emphasis of this chapter is on Type 2 diabetes. It has now become one of the major threats to human health in the 21st century.

An Epidemiological Perspective

The dramatic increase in the prevalence of diabetes (mainly Type 2) world-wide is a matter of enormous concern to individuals and public health authorities in both developed and developing nations and the World Health Organization (WHO).
Globally, the percentage of Type 2 diabetes is greater than 90 per cent. Type 1 diabetes is relatively uncommon in many populations, particularly Asian, Middle Eastern, the Pacific Islands and African.\(^1\) Not only is the prevalence increasing, but the age of onset of Type 2 diabetes is becoming younger with an increasing, but so far poorly quantified, number of children and adolescents now being diagnosed.\(^4\)

The changing perception of diabetes as a global public health threat relates partly to a better appreciation of its devastating complications, but mainly to the rapid, and unanticipated, rise in its prevalence that has occurred in the latter part of the 20th century. The evidence for this global rise is now clear. In Native American and Pacific Island populations, Type 2 diabetes now affects up to 40 per cent of adults,\(^5,6\) but was virtually unknown 50 years ago.

There has been an overwhelming number of studies of diabetes prevalence in the last few decades, again underlining the increasing interest in this chronic disease. Just to cite a few striking examples:

- Between 1976 and 1988, the prevalence of diabetes rose from 11.4 per cent to 14.3 per cent in the USA among people aged 40–74 years.\(^7\)

- Two cross-sectional studies in an urban south Indian population showed that the prevalence in the over-20s had risen from 8.3 per cent in 1989 to 11.6 per cent in 1995.\(^8\) For the year 2000, the prevalence in six major cities across India was reported to be 12.1 per cent.\(^9\)

- In China, the prevalence of 3.1 per cent in the over-25 age group was almost two and a half times higher than a figure from the Chinese province of Da Qing eight years earlier.\(^10\) By 2001, the prevalence amongst those aged 35–74 had further risen to 5.5 per cent.\(^11\)

- European studies are few, but Drivsholm and coworkers reported a 38 per cent rise in the prevalence of diabetes over 22 years.\(^12\)

- In Latin American countries, the crude prevalence of Type 2 diabetes in the year 2000 ranged from 1.2 per cent in Chile to 8.2 per cent in Argentina.\(^13\)

- In Africa, diabetes prevalence ranges from 0.7 per cent in rural Tanzania to 10.0 per cent in the Northern Sudan.\(^14\)

- In Australia, 7.4 per cent of adults now have diabetes compared with an estimated 3.4 per cent in 1981.\(^15\) Almost one in four Australians aged 25 years and over has either diabetes or a condition of impaired glucose metabolism. The prevalence has trebled over the last 20 years. Approximately 20 per cent of the population are affected by their late 60s.\(^15\)
It should be noted that many of the high prevalence figures reported in Pacific Island communities, including Asian Indians in Fiji, were from surveys performed over 15 years ago, yet these rates still remain amongst the highest yet recorded. More recently, a study during 1998 and 2000 by Colagiuri and coworkers revealed a prevalence of diabetes in Tonga of 15.1 per cent, of which 80 per cent was undiagnosed. A similar survey in 1973 reported a 7.5 per cent prevalence, indicating a doubling of diabetes over the past 25 years in this Polynesian paradise!

We have recently undertaken an analysis of worldwide data on diabetes prevalence rates. Figure 1.1 shows the top 10 countries for diabetes as reported in the Diabetes Atlas 2003.

A particularly worrying feature of the epidemic of diabetes has been the concurrence of glucose intolerance with other cardiovascular disease (CVD) risk factors. In the Australian Diabetes, Obesity and Lifestyle Study (or AusDiab), the presence of obesity, hypertension, elevated LDL cholesterol, low HDL cholesterol and elevated triglycerides (shown in Table 1.1) were dramatically increased in the

\[\text{FIGURE 1.1} \quad \text{The top 10 countries for diabetes prevalence (modified from reference 2)}\]

<table>
<thead>
<tr>
<th>Country</th>
<th>Crude prevalence (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nauru</td>
<td>30</td>
</tr>
<tr>
<td>Republic of Singapore</td>
<td>25</td>
</tr>
<tr>
<td>Kuwait</td>
<td>22</td>
</tr>
<tr>
<td>Reunion</td>
<td>20</td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>20</td>
</tr>
<tr>
<td>Cuba</td>
<td>18</td>
</tr>
<tr>
<td>Bahrain</td>
<td>18</td>
</tr>
<tr>
<td>Qatar</td>
<td>16</td>
</tr>
<tr>
<td>United Arab Emirates</td>
<td>15</td>
</tr>
<tr>
<td>Seychelles</td>
<td>15</td>
</tr>
</tbody>
</table>

*for adults aged 20–79

<table>
<thead>
<tr>
<th>TABLE 1.1 Prevalence (%) of CVD risk factors in Australia stratified by glucose tolerance status\textsuperscript{18}</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obesity (BMI ≥ 30 kg/m\textsuperscript{2})</strong></td>
</tr>
<tr>
<td>Hypertension (≥ 140/90 mm Hg)</td>
</tr>
<tr>
<td>LDL ≥ 3.5 mmol/l</td>
</tr>
<tr>
<td>HDL &lt; 1.0 mmol/l</td>
</tr>
<tr>
<td>Triglycerides ≥ 2.0 mmol/l</td>
</tr>
</tbody>
</table>

Data are not age or sex adjusted. Reproduced with permission from Shaw, JE and Chisholm DJ\textsuperscript{18}.
diabetic population compared with those with normal glucose tolerance.\textsuperscript{18} This concern regarding CVD risk becomes even greater when one considers that people with a lesser abnormality of blood glucose levels (impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)) have a substantial increase in CVD risk factors and an approximate doubling of cardiovascular risk.\textsuperscript{1,18} The association of glucose intolerance with other key CVD risk factors is known as the metabolic syndrome and this association is discussed in more detail later.

\section*{The Hidden Epidemic – Impaired Glucose Tolerance and Impaired Fasting Glycaemia}

Worldwide it is estimated that more than 350 million people have IGT or IFG.\textsuperscript{2} The Australian AusDiab Study recently surveyed the glycaemic status of a population of 11,247 adults.\textsuperscript{15} The combined prevalence of IFG and IGT was 16.4 per cent. These glucose-intolerant, but non-diabetic, individuals represent a large reservoir of potential new diabetes cases.

Impaired glucose tolerance was considered a separate class in the previous WHO classification but is now categorized as a stage in the natural history of disordered carbohydrate metabolism.\textsuperscript{19} Impaired fasting glycaemia (IFG) is now formally recognized, as these people also are at greater risk for progression to diabetes and macrovascular disease, although prospective data are sparse and early data suggest a similar risk of progression to diabetes as exists for IGT.\textsuperscript{20,21} IFG refers to fasting glucose concentrations that are lower than those required to diagnose diabetes mellitus but higher than the ‘normal’ reference range.\textsuperscript{19} IGT and IFG are not clinical entities in their own right but rather risk categories for future diabetes and/or cardiovascular disease.\textsuperscript{22} They represent impaired glucose regulation, which refers to a metabolic state intermediate between normal glucose homeostasis and diabetes. Both IGT and IFG are often associated with the metabolic syndrome.\textsuperscript{22}

The American Diabetes Association (ADA) has recently considered whether the lower limit for IFG should be reduced from 6.1 mmol/l (110 mg/dl).\textsuperscript{23} The ADA, on reviewing the data, suggested that the cut point for IFG should be reduced from 6.1 mmol/l (110 mg/dl) to 5.6 mmol/l (100 mg/dl), and that IFG should be redefined as an FPG of 5.6–6.9 mmol/l (100–125 mg/dl). If an OGTT is performed, some individuals with IFG will have IGT. Some may have diabetes, but this cannot be determined without an OGTT. If resources allow, it is recommended that those with IFG have an OGTT to exclude diabetes.\textsuperscript{22,23}

\section*{Glucose Intolerance and the Metabolic Syndrome}

The metabolic syndrome, also known as syndrome X\textsuperscript{24} and the insulin resistance syndrome,\textsuperscript{25} is a cluster of metabolic abnormalities (glucose intolerance,
hyperinsulinaemia/insulin resistance, central obesity, dyslipidaemia and hypertension) that occur together in an individual more often than might be expected by chance. They are associated with increased CVD risk, and in two studies from Europe\textsuperscript{26,27} the presence of the syndrome predicted increased cardiovascular and coronary heart disease mortality. Insulin resistance has been suggested as a single common cause for all of the components of the syndrome, and some studies have implicated it in this role, but this has not been confirmed in other work.

The putative central role of insulin resistance led to the labelling of the insulin resistance syndrome,\textsuperscript{25} whose features include insulin resistance, central obesity, dyslipidaemia (especially elevated triglycerides and reduced HDL-cholesterol), hypertension, hyperuricaemia and increased plasminogen activator inhibitor-1. The causative mechanisms involved have still not been precisely defined but one possibility is that central obesity and excess lipid availability constitute a major mechanism for many or all of these abnormalities.

There are currently several definitions of the syndrome in use, making it difficult to compare prevalence rates between countries. The World Health Organization (WHO) definition\textsuperscript{19} and the European Group for the Study of Insulin Resistance (EGIR)\textsuperscript{28} require glucose intolerance or insulin resistance as an essential component. However, for the ATPIII definition developed by the American National Cholesterol Education Program (NCEP)\textsuperscript{29} this is not the case. The cut points for each component and the means of combining components also differ.

A comparison of prevalence, applying the WHO definition of the metabolic syndrome\textsuperscript{19} among various populations worldwide\textsuperscript{30–34} is shown in Table 1.2. Even where studies involve participants within the same age range, there is a wide variation in prevalence between countries. A consistently higher prevalence is seen

<table>
<thead>
<tr>
<th>Country</th>
<th>Age group (years)</th>
<th>Reference</th>
<th>Prevalence (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Men</td>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>&gt;24</td>
<td>unpublished</td>
<td>25.2</td>
<td>16.7</td>
<td></td>
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<tr>
<td>Denmark</td>
<td>60</td>
<td>35</td>
<td>38.0</td>
<td>22.0</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>35–64</td>
<td>30</td>
<td>23.0</td>
<td>12.0</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>40–81 F</td>
<td>35</td>
<td>34.5</td>
<td>18.0</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>46–68</td>
<td>35</td>
<td>43.3</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>Mauritius</td>
<td>&gt;24</td>
<td>32</td>
<td>20.9</td>
<td>17.6</td>
<td></td>
</tr>
<tr>
<td>Occupied Palestinian</td>
<td>30–65</td>
<td>36</td>
<td>Total = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Territories</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td>50–69</td>
<td>37</td>
<td>24.6</td>
<td>17.8</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>40–74</td>
<td>33</td>
<td>41.3</td>
<td>32.7</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>30–79</td>
<td>34</td>
<td>30.3</td>
<td>18.1</td>
<td></td>
</tr>
<tr>
<td>USA (non-Hispanic white)</td>
<td>30–79</td>
<td>34</td>
<td>24.7</td>
<td>17.2</td>
<td></td>
</tr>
<tr>
<td>USA (Mexican American)</td>
<td>30–79</td>
<td>34</td>
<td>32.0</td>
<td>28.3</td>
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</tbody>
</table>
among men, with almost all studies finding a prevalence higher than 20 per cent. For women, most populations had a prevalence of less than 20 per cent.

**Globalization – Its Impact on Human Health**

Globally there has been a small but important increase in the incidence of Type 1 diabetes (which will be discussed elsewhere in this issue) but a massive explosion of Type 2 diabetes.² What is the reason for this phenomenal increase? Although we do not have all the molecular answers, the epidemiological data seem clear. Type 2 diabetes is a lifestyle disorder, and during the last 30–40 years there have been dramatic changes in the human environment, behaviour and lifestyle, which have resulted in escalating rates of obesity and diabetes.¹,³⁸ More recently, the term diabesity has become fashionable to describe the association of obesity and Type 2 diabetes.¹

Genetic influences are clearly important, with a strong familial tendency and also major ethnic differences in prevalence.¹⁶,³⁹ In the Pacific region, the Micronesians in Nauru, Polynesians in Samoa³⁹ and Tonga¹⁷ and our own Australian indigenous population have especially high risk.⁴₀ Asian Indian and Chinese who have moved to urban centres or to developed nations also have a relatively high risk, though the particular predisposing genes have defied identification.³⁹ The highest rates in the world have been consistently found among Native American populations.⁴¹

The genetic aspect forms a background to massive changes in the human environment. A favoured theory to explain the unduly high risk in some populations relates to a ‘thrifty genotype’. Historically, this genotype permitted populations such as the Polynesians in the Pacific to survive long famines, unfavourable environments and migration by favouring energy conservation and fat accumulation.⁴²,⁴³ The proposal is that these communities had genes that allowed increased fat storage in times of feast, but result in obesity, hyperinsulinaemia and Type 2 diabetes in the transition to a modern lifestyle characterized by sedentary activity and relative over-nutrition.⁴³ The Western lifestyle appears to unmask the effects of pre-existing genes because the consistent result has been diabetes within a few decades.⁴³ An alternative theory, proposed by Hales and Barker,⁴⁴ suggests that foetal nutritional deprivation, with low birth weight, is a major predisposing factor to the later development of the insulin resistance syndrome and Type 2 diabetes. Their proposal remains controversial as statistically it may explain only a small proportion of the diabetic risk. Also, the association of low birth weight with diabetic risk in later life could be related more to genetic rather than nutritional factors, in fact another example of the thrifty gene scenario.⁴³

Jared Diamond, a leading American biologist and author, has suggested that the lifestyle-related diabetes epidemic in Native Americans and Pacific Islanders probably results from the collision of our old hunter–gatherer genes with the
new 20th century way of life.\textsuperscript{45} He has recently taken this further, raising the question of why it is that while Type 2 diabetes is exploding in prevalence, despite its obvious selective disadvantage, some human populations are much more affected than others.\textsuperscript{46} The epidemic seems well established in most parts of the world except in Europe.\textsuperscript{2} Diamond suggests that part of the answer may lie in Europe’s recent food history and the genetic and evolutionary consequences of geographic differences in food history.\textsuperscript{46}

**Type 2 Diabetes in Children and Adolescents**

One of the most alarming consequences of the diabetes epidemic is the appearance of Type 2 diabetes in children and adolescents.\textsuperscript{2,47} Until a decade or so ago, Type 2 diabetes was regarded as a disease of the middle aged and elderly. While it still is true that this age group maintains a higher relative risk (in relation to younger adults), there is accumulating and disturbing evidence that onset in the 20–30 age group is increasingly seen.\textsuperscript{47,48} Now, even children are becoming caught up in the Type 2 diabetes epidemic. Although Type 1 diabetes remains the main form of the disease in children worldwide, it is more than likely that within 10 years Type 2 diabetes will be the more prevalent form in many ethnic groups, potentially including Europid groups. There are now numerous reports of Type 2 diabetes in children from countries including Japan, the United States, Pacific Islands, Hong Kong, Australia, the United Kingdom and Taiwan.\textsuperscript{47–51} Dabelea and coworkers have reported on changes in rates of diabetes in Pima Indian children over a 30 year period.\textsuperscript{52} They have demonstrated rising rates of glucose intolerance with time, and age as well as a female preponderance. From 1967–76 to 1987–96 the prevalence of Type 2 diabetes in children markedly increased from 2.4 per cent in males and 2.7 per cent in females to 3.8 per cent in males and 5.3 per cent for females.

The emergence of Type 2 diabetes in children brings a serious new aspect to the diabetes epidemic and heralds an emerging public health problem of major proportions in the paediatric area. The rise of Type 2 diabetes in this age group is mainly due to the increase of time spent on sedentary activities such as television and computer usage, either for games or school-work, with consequent reduction in sports. Add to this the increasing availability of energy-dense foods, high in saturated fats, and we have a ‘witches’ brew’ to promote obesity and Type 2 diabetes. Type 2 diabetes in children is usually associated with obesity and a strong family history, and often with acanthosis nigricans and polycystic ovarian syndrome. Among children in Japan, Type 2 is already more common than Type 1 diabetes, accounting for 80 per cent of childhood diabetes; the incidence almost doubled between 1976–80 and 1991–5.\textsuperscript{48} The rising prevalence of obesity and Type 2 diabetes in children is yet another symptom of the effects of globalization.
and industrialization affecting all societies, with sedentary lifestyle and obesity the predominant factors involved.1

This fall in the age of onset of Type 2 diabetes is an important factor influencing the future burden of the disease. Onset in childhood heralds many years of disease and an accumulation of the full range of both micro- and macrovascular complications.1 The ADA and the American Academy of Pediatrics have published a consensus statement on the problem.49 A key area raised in this report is the issue of poor compliance in diet and in tablet and insulin therapies. Recently, a number of pharmaceutical companies have embarked on clinical trials of oral hypoglycaemic agents to check their safety and efficacy in this age group, as they may face up to 40–50 years of therapy. Another worrying aspect is the high risk of, and early appearance of, long-term micro- and macrovascular complications in the adolescent and early adult years. The socio-economic and public health impact of this shift toward younger disease onset will be considerable through effects on the size of the fit and able work-force, premature morbidity and mortality and the negative impact on fertility and reproduction.

Prevention – The Reality and the Challenge

It does not come as a surprise, given the dramatic increase in Type 2 diabetes and its complications, and its socio-economic impact worldwide, that there is now a major interest in primary prevention. A number of studies discussed elsewhere in this book have clearly demonstrated that lifestyle modification (weight reduction and increased physical activity) can dramatically reduce the incidence of Type 2 diabetes in high-risk subjects. Unfortunately, the intensity of effort and associated costs in the two major studies in developed countries, the Finnish Diabetes Prevention Study,53 and the American Diabetes Prevention Program,54 may not permit implementation on a community-wide basis.

The use of pharmacological agents for Type 2 diabetes prevention is also being explored and, while contrary to an appropriate community-based lifestyle intervention strategy, may be contemplated where lifestyle intervention fails or is difficult from a socio-cultural perspective.55 Although preventive action will not be easy or cheap, the magnitude of the problem we face with diabetes and its complications demands serious action.

References

REFERENCES

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