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he US Centers for Disease Control and Prevention recently claimed that more than 1 in 3 American adults have blood sugar levels that are too high.¹ They included prediabetics in their statement.

In 2016, the University of California, Los Angeles (UCLA), reported that 55% of Californian adults are either prediabetic or have undiagnosed type 2 diabetes (Figure 1).² Prediabetes is not a nit-picking philosophical concept. Diabetic pathologies develop during prediabetes³ and, by the time type 2 diabetes manifests itself, patients may already have kidney impairment,^{4,5} vision loss,⁶⁻⁸ neuropathy,⁹ atherosclerosis¹⁰⁻¹² and cancer.¹³⁻¹⁵ Excessive food and drink intake, particularly the high glycaemic ones, spike blood sugar levels which also accelerate ageing by shortening telomeres.^{16,17}

The goalposts for safe blood glucose levels have been changing. Levels considered dangerous now were thought to be safe decades ago. Current recommendation is for blood sugar to be kept at the low end of the normal reference range.¹⁸⁻²¹ However, a significant section of the medical community may have failed to wake up to the life-shortening impact of prediabetes.

One diagnostic problem is that prediabetes and early stage diabetes may be missed by the standard fasting blood glucose in the presence of hyperinsulinaemia. As long as there is reasonable insulin sensitivity and hyperinsulinaemia, a fasting blood glucose may appear to be in a safe range, which is conventionally considered to be under 5.6 mmol/L, although some claim the safe upper limit ought to be 4.7mmol/L.

Hyperinsulinaemia contributes to disease states (e.g. hypertension, blood hypercoagulability and increased cancer risk) even before fasting blood glucose rises to what conventional medicine regards as prediabetic levels, namely, 5.6 – 6.9 mmol/L. For the above reasons, and in this scenario, the fasting blood glucose test should perhaps now be considered dangerously obsolete.

The haemoglobin A1c (HbA1c) blood test provides a better picture of glycaemic control than fasting blood glucose,²² but is probably underutilised in identifying prediabetes. The safe upper limit for HbA1c is considered 5.5%, but lower ranges have been shown to be healthier.²³ HbA1c between 5.6% and 6.4% is diagnostic for prediabetes.²⁴

> EXCESSIVE FOOD AND DRINK INTAKE, PARTICULARLY THE HIGH GLYCAEMIC ONES, SPIKE BLOOD SUGAR LEVELS WHICH ALSO ACCELERATE AGEING BY SHORTENING TELOMERES



Metformin ought to be prescribed when the HbA1c is between 5.6% and 6.4% for prevention of type 2 diabetes,²⁵ together with advice on calorie restriction and, in particular, the high glycaemic ones. Metformin enhances insulin sensitivity and functions via several mechanisms to improve glycaemic control.²⁶⁻³⁰ It has proven ability to delay or prevent type 2 diabetes.³¹⁻³³ Yet recent US surveys reveal it is prescribed to only 3.7% to 8.1% of prediabetics.³³⁻³⁵

Perhaps the term prediabetes is a misnomer because even modestly elevated glucose levels inflict microvascular damage resembling the long-term complications of type 2 diabetes.^{36,37} Excess glucose is converted to triglycerides that are stored as fat (subcutaneous and abdominal) and which may result in fatty liver disease (may progress to cirrhosis and hepatocellular carcinoma). Excess glucose is inflammatory to many tissues, including arteries (atherosclerosis).³⁸⁻⁴⁰ High "normal" blood sugar levels are increasingly recognised as posing an increased risk of degenerative disorders.^{4-15,20,41-49}

Fasting blood glucose values in the upper "normal" range (above 4.7mmol/L) appear to be an important independent predictor of cardiovascular death in nondiabetic, apparently healthy, middle-aged men.¹⁸ After-meal glucose levels are an even stronger predictor of disease risk.⁵⁰⁻⁵²

About 70% of prediabetics will develop type 2 diabetes in their lifetime.^{53,54} It is misleading to think that prediabetes relates to a period where no diabetic damage is caused. Coronary heart disease risk is similar between prediabetics and type 2 diabetics.⁴⁷

EARLY DETECTION OF PREDIABETES MEANS A GREATER LIKELIHOOD OF REVERSING IT BEFORE IT PROGRESSES TO TYPE 2 DIABETES

Early detection of prediabetes means a greater likelihood of reversing it before it progresses to type 2 diabetes. Glucose-lowering approaches should be initiated when HbA1c exceeds 5.5% and not delayed till it reaches 6.5%.

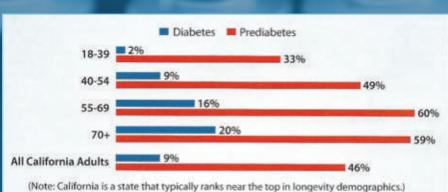
In the area of laboratory predictive testing for cardiovascular risk, we have probably underestimated the importance of the prediabetic state (as defined by HbA1c levels above). For around 60 years we accepted the hype around cholesterol, dietary saturated fats, heart attacks and now, statins. In spite of the huge global expense on cholesterol testing and statins, atherosclerotic-related morbidity and mortality remains number one in industrialised countries.

The clinical significance of the various blood lipoproteins is still confused. We now know that there are at least two main types of LDL cholesterol, a small, dense atherogenic particle and a larger lighter one thought to be harmless. The different LDL particles are too expensive to be measured routinely. We therefore don't know whether a high LDL is due to an elevated "harmless" or "bad" LDL sub-fraction. Adding "non-HDL cholesterol" to routine testing is even more confusing. The combination of a raised fasting triglycerides level and a low HDL level is a surrogate marker for raised "bad" LDL (see previous features in the *The Synapse Journal* on the Cholesterol Controversy). What raises fasting triglycerides levels and lowers HDL are high glycaemic carbohydrates and alcohol, rather than saturated fats.

> MALTA HAS ALMOST THREE TIMES THE HEART DISEASE MORTALITY OF FRANCE ... OBESITY AND BLOOD GLUCOSE LEVELS MIGHT BE THE MAIN PROBLEM, RATHER THAN CHOLESTEROL

Glucose may be a more important damaging inflammatory agent than saturated fats. The French have the lowest heart disease mortality in Europe (and second lowest worldwide). Malta has almost three times the heart disease mortality of France. The reason is not Maltese consumption of dairy produce and meats being three times that in France. Obesity and blood glucose levels might be the main problem, rather than cholesterol. Perhaps about half our adult population is prediabetic or already diabetic, like California. Who knows?

The term "prediabetes" may render a false sense of normality. Perhaps the progression stages of type 2 diabetes could more realistically be renamed, "early diabetes", "established diabetes" and "end-stage (insulindependent) diabetes". A false sense of normality is also fostered by laboratories in Malta stating a "normal range" for HbA1c of up to 6.5%, when it should be up to 5.5%.



Source: 2013-14 California Health Interview Survey

Figure 1: Diabetes cases by age group. A UCLA study found that 55% of adults in California have either diabetes or prediabetes.²

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