

ACADEMIC: CASE STUDY

“What’s the damage? Give it to me!”: Type 2 diabetes mellitus and obesity management in primary care with implications for biomedical science, clinical practice and population health

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Human frame—A story

Soft drizzle greets me as I make the short, familiar dash between the train station and the general practice where I will spend the next month of my fifth year of medical school. As I walk up the main street, which I have all to myself at this time of day, I spy no fewer than 30 dairies, fast food outlets or liquor stores in hardly 500 metres—I know because I count them each morning.

It's a Thursday which means I will be sitting in with the lead practice nurse and resident diabetes expert, Deepa. We're in for a busy morning, as always. My first acquaintance with our first patient occurs as we bring up her blood results. Deepa's brow furrows as she graphs the HbA1c. It has remained stubbornly elevated for the past five years and today is no exception.*

A few moments later, Anahera shuffles in, asking with defeated animation, “What’s the damage? Give it to me!” Deepa tries to remain measured and upbeat even though it is clear that the numbers other than the cholesterol are showing no signs of improvement. There is talk of filling half the dinner plate with vegetables among other “lifestyle” interventions. We all nod in enthusiastic synchronicity, but I can't help but feel we are nodding in complicity with disease progression.*

When Deepa leaves the room momentarily, I have the urge to counter what I perceive as Anahera's deflated sense of agency, but my words fail me. Anahera shares more about her hectic work and what sounds like a back-breaking work roster. We share a warm, knowing smile as we agree that sometimes after a hard day's work, there's nothing quite like a pie. The irony that the aromas of freshly baked pies from the encircling bakeries are practically wafting into our consultation room is not lost on me.

Introduction

Type 2 diabetes mellitus (T2DM) is a condition that defines medicine in the 21st century. Multifactorial individual and environmental causes have given rise to a non-communicable disease that challenges traditional prevention and treatment paradigms. In this report, I explore the case of one patient with T2DM I met during my general practice

placement in South Auckland. I argue that in the face of such interwoven challenges, an understanding spanning from the pathophysiology to the pathological environment—and an ability to bridge these understandings in the clinical context—is essential in supporting patients with this complex condition.

Type 2 diabetes mellitus: an exemplary 21st-century disease

T2DM is an exemplary model of modern disease, comprising many elements of complex non-communicable diseases that characterise current clinical practice. An interplay of genetic, epigenetic, behavioural, and environmental causes gives rise to disordered glycaemic control that impacts people at all points of the lifespan.¹ Individual patient care involves several strategies including health promotion, secondary prevention, and medical and surgical interventions. T2DM's myriad complications require input from increasing numbers of medical specialties and other health professionals across community and hospital settings, presenting challenges for traditional health system organisation. At the population level, inequities are—unacceptably—evident both between and within countries, consistently disproportionately affecting marginalised populations such as Indigenous peoples and those with lower socio-economic status. Perhaps most significantly, T2DM need not be an inevitability. Population health strategies that prevent and control this condition whilst promoting equity are both plausible and imperative, particularly as scientific and technological innovations in the near future offer promising developments.¹

Case

Anahera is a 46-year-old Māori female healthcare worker and mother who presents at the nurse-led general practice clinic for an annual T2DM review.

Anahera was diagnosed with T2DM in June 2017, at which point her HbA1c was 62 mmol/mol. In addition to commencing metformin 500 mg twice daily, the notes record she was “motivated to make healthier lifestyle changes to improve diabetes... [and] quit smoking successfully.” Since then, her HbA1c has fluctuated between 52 mmol/mol in early 2018 to 72 mmol/mol in mid-2020 and was most recently 64 mmol/mol in June 2022. She is currently prescribed galvumet (vildagliptin 50 mg + metformin hydrochloride 1000 mg) twice daily but has only been taking the evening dose due to nauseating side effects. She has never taken insulin. She has been diagnosed with diabetic retinopathy, which is due for review in June 2023, but has not

suffered any other complications to date. She reports no concerns about her mood.

Her past medical history includes hyperlipidaemia managed with atorvastatin 10 mg nocte. She has no known allergies. There is a significant whānau history of hypertension, T2DM, and gout, each of which afflicts both parents and her siblings.

Anahera works in healthcare, requiring her to work up to ten consecutive days in 12-hour shifts. She reports finding it challenging to eat healthily as she gets home exhausted after a shift, although positively her job inherently involves substantial walking. She lives with her teenage children, and is looking forward to heading out of town with them for a week of reconnecting with whānau. She has reduced her cigarette consumption to three daily but is not yet ready to quit, and has started on nicotine replacement therapy. She drinks socially and does not report recreational drug use.

On examination, her height is 168 cm and weight 98 kg, giving a body mass index (BMI) of 34.7. Her blood pressure is 160/90 (last recorded at 130/94 in May 2021), and her pulse is 80 and regular. Her feet are warm and well-perfused, with palpable pedal pulses, well-trimmed nails and no evidence of peripheral oedema. There is intact sensation to 10 g monofilament bilaterally.

Her complete blood count, liver function tests, renal function tests, and urinary albumin-to-creatinine ratio are normal. Her lipid profile has normalised to within acceptable parameters since the last test, which showed a pattern of hyperlipidaemia.

A plan was made for further review of her blood pressure to consider initiation of medical treatment. Healthy eating, exercise, and smoking cessation were discussed, and the flu vaccine was offered but declined.

Discussion

Anahera's case raises several clinical questions around mitigating microvascular complications, optimising glycaemic control, and managing concurrent obesity and T2DM. In this discussion, I will explore this latter clinical problem using cellular, clinical, and societal lenses, illustrating that the pathophysiology and environmental context are inseparable from Anahera's presentation and management in primary care, and therefore constitute clinical problems that warrant our attention as clinicians.

DIABESITY: TOUCHING THE SURFACE OF AN INTERWOVEN PATHOPHYSIOLOGY

First, let us consider the cellular changes that may have contributed to Anahera's presentation of concurrent T2DM and obesity. Our understanding of the pathophysiology linking obesity and T2DM is becoming increasingly nuanced. Fundamentally, T2DM arises from a combination of defects in insulin secretion by pancreatic β -cells, and its action on muscle, liver, and several other organs.² At increasing BMIs, the corresponding increase in adipose mass mediates several deleterious changes impacting both insulin secretion and resistance.^{2,3} As an example of this latter effect, in adiposity, an abundance of freely circulating lipids disrupts physiological insulin signalling, such as the phosphoinositide 3-kinase pathway in muscle and other tissues that is essential for peripheral glucose uptake and therefore normalising blood glucose.^{3,4} Adipose tissue additionally secretes pro-inflammatory adipokines such as tumour necrosis factor alpha and interleukin six, which likely compound these effects. Mitochondrial dysfunction and endoplasmic reticulum stress induced by excess adipose tissue may further contribute to insulin resistance.⁵

Additionally, profuse lipids may "compete" unfavourably with glucose, disturbing normal insulin secretion. The "glucose—fatty acid cycle" hypothesis proposes that lipids rival glucose for peripheral metabolism, disrupting sensitive homeostatic loops that determine insulin release.⁵ Similarly, lipids directly stimulate β -cell insulin secretion, but chronic exposure can interfere with the role of glucose in this process.^{5,6} On the molecular level, genome-wide association studies have identified innumerable genetic variants associated with the development of obesity and/or T2DM.⁵ However, their mechanisms of

pathogenesis, relative effects, and inter-individual variation have proven difficult to elucidate, limiting their definitive explanative value to date.⁵ Epigenetic effects such as developmental programming may add yet another layer of complexity.^{3,5}

NEEDLESS DETAIL OR NECESSARY CHANGE? APPLYING SCIENCE IN THE CLINIC

Adapting clinical practice in response to this evolving disease paradigm is more critical than ever for providing evidence-based care to patients like Anahera. Whilst our understanding of the pathophysiology of T2DM may be expanding rapidly, this knowledge requires clinical application to improve patient outcomes. This may require scientists to be as adept at science communication as scientific methods.⁷ Meanwhile, clinicians will need to remain agile in a changing landscape, prepared for and supported to undertake continual processes of unlearning and relearning as increasing complexity in our biomedical understanding of disease reflects clinical decision-making that is less cut-and-dry.⁸

Anahera's case illustrates the importance of adapting to these new paradigms. One clinically relevant inference from an understanding of T2DM's pathophysiology is that there is a dose-response relationship between adipose weight gain and T2DM risk.⁹ This conclusion is reflected in several clinical observations. One study found that weight gain of one BMI unit between the ages of 25 and 40 increases the relative risk of T2DM by 25%, even at normal BMIs.^{5,10} Further evidence revealed that females with a BMI in the upper-normal range were four to five times more likely to develop T2DM than females with a lower-normal BMI, with similar findings in males.^{10,11} In this way, T2DM risk increases with an increasing adipose weight gain even within normal BMIs. Therefore, the optimal window to initiate primary prevention may occur long before a patient is overweight. Yet, current BMI guidelines in Aotearoa New Zealand fail to reflect this risk, stratifying individuals as underweight, normal, overweight, or obese, with only the latter two categories flagging clinical concern in guidelines.¹²

LOOKING BEYOND THE HUMAN BODY AND HEALTH SYSTEM: THE OBESOGENIC ENVIRONMENT

Looking within the human body provides explanations about the nature and mechanisms of obesity and T2DM, in turn generating implications for clinical practice. However, we must turn to Anahera's environment to understand some of the primary drivers of these concomitant conditions. Obesity has been characterised as a physiological response to an abnormal, obesogenic environment.¹³ Consumption-driven economic philosophies and policies have contributed to human development on some fronts, but one consequence has been a rapid transformation of the food system that is highly conducive to obesity.^{13,14} In developed countries, supply, distribution, and marketing changes make delicious but unhealthy food ubiquitously accessible.¹³ Mediators such as sociocultural norms, opportunities for active transport and recreation, and features of the built environment moderate the population impact on obesity and in turn T2DM, given obesity is the single most significant modifiable risk factor for T2DM.^{5,13} These forces invariably confluence with more proximal social determinants of health such as socio-economic status to determine the impact on individuals such as Anahera.¹⁵

Within this environmental context, strategies traditionally used in primary care, such as health promotion about diet and exercise, are still relevant in individual management.¹³ Whilst these interventions do not tend to attract controversy, they do not impact the underlying drivers of obesity and their efficacy depends on the aforementioned environmental mediators. In contrast, addressing the origin of the problem may require political leaders, working with experts, to take population health-based approaches to enact policies and regulations that primarily shape environments, not individuals. However, because these decisions often confront corporate interests and public inertia, worldwide implementation of effective policies to reverse the obesogenic environment has been slow.¹³

A SIZEABLE TASK: MANAGING OBESITY AND T2DM IN PRIMARY CARE

Primary care lies at the crossroads of this evolving understanding of pathophysiology and a pathological environment. On the one hand, understanding biomedical science seems to point to the virtuous conclusion that to prevent T2DM, notwithstanding pathological underweight states, any adipose weight gain would ideally be mitigated. This must be reconciled with the reality that our environments are conducive to the exact opposite, namely weight gain. In this seemingly impossible position, what role does primary care play?

Primary care management of non-communicable diseases such as T2DM typically comprises screening and health promotion, primary and secondary disease prevention, and non-specialist disease management.¹⁶ This is reflected in primary care's central role in Anahera's T2DM journey. Since making the diagnosis, the general practice has managed her medication; conducted brief lifestyle interventions regarding smoking cessation, diet, and exercise; treated her co-morbid hyperlipidaemia and hypertension; and monitored for end-organ complications. A more difficult question is whether this role remains a reasonable expectation in the face of such rapid evolution of both the scientific underpinning and environmental context of clinical practice.

The importance of primary care in the management of obesity and T2DM is both recognised and realised by its workforce. Qualitative research with New Zealand general practitioners (GPs) revealed that most believed primary care has a fundamental role in managing obesity and T2DM.¹⁷ GPs thought it was within their remit to identify the issue, provide health promotion, and leverage their role as health professionals to act as a positive influence and motivating force in patients' lives.¹⁷ Evidence suggests GPs do routinely and opportunistically raise the importance of weight management despite the potentially difficult nature of the conversation.¹⁸ Furthermore, GPs have positive attitudes and moderate confidence in providing nutrition advice.¹⁹ Ultimately, GP health promotion efforts of this nature can be characterised as encouraging, supporting, and celebrating sustainable long-term lifestyle changes, however small they may be.¹⁷⁻¹⁹

However, a variety of factors including the environmental drivers previously outlined make the effective management of obesity and T2DM increasingly challenging—and perhaps demotivating for both clinicians and patients. Due to patient and resource factors, New Zealand GPs report feeling disempowered when addressing weight loss.¹⁷ GPs identified individuals' social determinants of health, such as poverty and socio-cultural beliefs, coupled with insufficient resources both within and external to the health system as barriers to achieving progress. Additionally, they expressed doubts about the efficacy of primary care management for weight loss.¹⁷ Unfortunately, these reservations seem to be confirmed given that weight loss interventions targeting both diet and physical activity positively impact weight up to the first 24 months, with scant longer-term evidence of efficacy.²⁰ Furthermore, weight loss interventions targeting only one of these factors were not supported by evidence of long-term effectiveness. Finally, GPs held mixed views about more intensive interventions such as bariatric surgery, recognising that the root causes of obesity remain unaddressed.¹⁷ In this way, T2DM challenges traditional primary prevention strategies used in primary care. Clinical practice and health system organisation will need to adapt and innovate to remain responsive to the environmental drivers of diabetic presentations.²¹

Conclusion

T2DM is a complex condition that exemplifies the inextricable nexus between pathophysiology, clinical medicine, and the social determinants of health. For the clinician, the evolving paradigm of T2DM challenges traditional, comfortable ways of working. It demonstrates that changes spanning from the cellular to the societal are critical for understanding the patient in front of us, and their clinical presentation and problems. With this comes an obligation to integrate clinical factors alongside a consideration of biomedical evidence and an understanding of our patient's environment into clinical decision-making.

Faced with such challenges, scientists, clinicians, public health experts and other stakeholders need to be able to work collaboratively along this disease spectrum. The ability to drill down into one's area of deep expertise is as important as the capacity to step back, place one's contributions within the broader context, and share them using a common language. This transdisciplinary synergy at the intersection of biomedical research, clinical medicine, and population health may be more critical than ever in generating effective avenues to prevent and manage this disease, ultimately achieving our shared mission to uplift the health of individuals and populations.

Human frame—A reflection

After a long but stimulating day, the sun has finally emerged as I retrace the streets that lead back to the station. Reflecting on the patients and their stories, I am both daunted by the challenges T2DM poses to individuals, communities, and our world, but equally inspired by the potential to make a world of difference.

My conversation with Anahera resurfaces in my mind. I feel despondent when I think of the powerful forces that have shaped her trajectory to date, but I remain hopeful that maybe, just maybe, we achieved something positive today. I realise that Anahera has taught me so much about health and disease, clinical medicine, life, and my place amongst it all. Whizzing past traffic jams and backyards with children playing from my vantage point on the train, I conclude that our mission is at once infinitely complex, elegantly simple, and above all deeply meaningful:

Healthy people thrive in healthy environments.

Anahera and the people of South Auckland deserve that, and so much more.

*Patient consent and confidentiality: Written consent was obtained from the patient for their anonymised details to be published in this case report. Some details were changed to preserve anonymity.

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