

REFLECTIONS

The University of Cape Town taught me how to challenge beliefs

Timothy David Noakes

The world's first successful human heart transplantation on 2 December 1967 inspired me to study medicine at the University of Cape Town's Faculty of Health Sciences. There I learned 5 key elements for a successful career in either medicine or science or both – perfectionism, passion, compassion, the dispassionate investigation of all the available evidence, and the need to challenge established beliefs for which the scientific evidence appears imperfect. Challenging such beliefs enabled us to prove that hyponatraemic encephalopathy

was caused by persistent and heroic over-drinking during prolonged exercise, usually lasting more than 4 hours, and was unrelated to salt losses in sweat and urine; to understand that the brain not the muscles must regulate the exercise performance, and thus develop the Central Governor Model of Exercise; and to reconsider the dietary causes of the obesity and diabetic epidemic.

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On 3 December 1967, while in the USA, I heard the radio news that changed my life. A South African heart surgeon, Dr Christiaan Barnard, had performed the world's first successful human heart transplant at Grootte Schuur Hospital in Cape Town. I began my medical training at the University of Cape Town (UCT) in 1969 and am forever grateful to Dr Barnard and his team. He wrote: 'Most of us think along straight lines, like a bus or a train or a tram. If the destination isn't up on the board, few of us would know where we are going – and that applies even to scientific researchers who should know better. We tend to let traditions lead us by the nose. It takes an effort of will to break out of the mould.'¹

UCT Medical School in the 1970s

A moment to objectively review the influence of our education in the 1970s at the UCT Medical Faculty was the 30th reunion of our graduating class in December 2004. My outstanding impression was of the extraordinary achievements of our class in careers spread around the globe and I realised the extent of the influence graduates of the Faculty must have had over the past 100 years. Since we knew our strengths and weaknesses, we concluded that these achievements were not because we had special attributes. Rather the basis must have been the education to which we had been exposed and the quality of the teachers who taught me 3 key lessons.

The first was to aim for perfection, without which we placed our patients' lives at risk. Later I learned from the great American football coach, Vince Lombardi: 'Winning is not a sometime thing here. It is an all-the-time thing. You don't win once in a while, you don't do things right once in a while, you do them right all the time. Winning is a habit. Unfortunately so is losing.'² Teachers taught us to be thorough in whatever we did – either we did it right all the time or else just as well not do it. Secondly, remarkable teachers were passionately involved in what they did – they were consumed by their work and desire to share

their passions. To make a difference, each needed to discover, and pursue for life, our particular passion. Thirdly, compassion – perhaps the single feature that distinguished the truly exceptional teachers – those with real, not phony, compassion that drew us to them. Teachers who became our ultimate role models combined all 3 characteristics.

Choosing an area of specialisation

In my first year discovering endurance sports became the defining influence in my life, and there was no way back into conventional medicine.³ In my fourth year I met Professor Lionel Opie, who provided the fourth key lesson: our beliefs and practices should be based on the best available evidence. This requires exhaustive investigation of the literature to ensure that our truths are based on the total evidence, or we may espouse a wisdom created to serve another, less noble agenda.⁴ Opie's remarkable books^{5,6} are examples of scientific perfectionism in exposing the bedrock of truth. After internship I joined his Heart Disease Research laboratory to become a medical scientist, where he taught me the fifth key lesson – to challenge existing beliefs.

Developing a scientific endeavour

Having completed my doctoral training I received a letter from an athlete who had developed a grand mal seizure after the 90 km Comrades marathon in 1981. She had been hospitalised in Durban as the world's first recorded case of exercise-associated hyponatraemic encephalopathy (EAHE).^{3,7} By 1991 we had proved that EAHE was caused by persistent over-drinking during prolonged exercise, usually lasting more than 4 hours, and was unrelated to salt loss in sweat and urine.⁸ We later found that EAHE requires inappropriate ADH secretion – the syndrome of inappropriate ADH secretion (SIADH) – and perhaps abnormal regulation of the exchangeable sodium stores.⁹ Therefore, to prevent the condition athletes should drink only according to their internal biological signals, i.e. thirst, and not according to rigid guidelines set by compliant scientists, many with undisclosed links to the sports drink industry.^{3,10} Unfortunately our findings were relegated to the background when the sports drink industry in the USA decided to increase its product sales by promoting a novel fantasy: the 'science of hydration'.^{3,10} Its 3 pillars are: dehydration is a 'dread disease' that impairs exercise performance, causing muscle cramps and an increased risk of a fatal 'heat illness'; these risks can be reduced only by drinking 'as much as tolerable' and staying 'ahead of thirst' during exercise; and EAHE occurs in those who lose abnormally large amounts of sodium in their sweat, so-called 'salty sweaters', and can be prevented by ingesting large volumes of sodium-containing sports drinks during

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exercise. Ultimately, the truth established in 1991, that drinking according to the dictates of thirst prevents EAHE,¹¹ and that sodium ingestion plays no role,¹² could no longer be suppressed.¹⁰

My second area of interest was stimulated in 1981 by Professor Wieland Gevers. Lecturing to our inaugural class of BSc Honours Sports Science students, begun under his mentorship, he commented that we should never believe that muscles necessarily become oxygen-deficient during exercise. At that time this seemed utterly improbable, but his words were later proved correct.

The original teaching in the exercise sciences presumes that the exercising body is 'brainless'.¹³ Once we realised that the brain, not the muscles, must regulate exercise performance, we could develop the Central Governor Model of Exercise.^{3,14} This model proposes that the body acts as a complex system during exercise, with the brain ensuring that homeostasis is maintained and that exercise terminates before there is a catastrophic biological failure.

The paradox of the rise of received wisdom despite an increase in research

The amount of scientific research being undertaken has increased exponentially. Few opportunities existed when I began, as our Faculty was yet to consider research a critical enterprise, whereas today aspiring medical scientists can pursue a wide range of choices. It seems that a critical mass of research excellence has now been surpassed.

We have now reached the paradoxical situation: global medical research has grown exponentially, yet it is probable that much public health information propounded as undeniably 'true' is manufactured to serve the commercial interests of several global industries.^{15,16}

My clash with the multibillion dollar-a-year US sports drink industry^{3,10} taught me that medical science can as easily be bent to serve commercial interests as it can be used to produce 'the greatest benefit to humankind'.¹⁷ Too many medical 'truths' are decided by industries that generate products, especially pharmaceutical agents, on which our profession has become too dependent. This relationship has promoted falsehoods with devastating consequences. One instance relates to the causes of obesity and adult-onset (type II) diabetes. In 1963 Campbell¹⁸ showed that the appearance of diabetes in Zulu-speaking urban-dwellers and Indian immigrants to Durban was associated with adopting a diet with an increased sugar intake, also confirmed in other populations.^{19,20} The rising incidence of diabetes occurred within about 20 years of first adopting the 'white man's diet', in keeping with the classic observations by Price²¹ that population health falls immediately as it adopts a diet including refined carbohydrates in the form of sugar and white flour. Indeed, the introduction of agriculture, replacing foods with higher fat and protein content with carbohydrate-rich cereals, was associated with a loss of height in humans between 5 000 and 12 000 years ago.²²

The mass extermination of the bison, their main foodstuff, by white men led to the rapid loss of height of the Plains Indians in North America, formerly the tallest and healthiest of all North Americans.²³ They descended into epidemic obesity and diabetes,²⁴ as they failed to adapt to a high-carbohydrate diet comprising mainly sugar and white flour.²⁵ This same phenomenon has overtaken most North Americans on a high-carbohydrate diet with a reduced intake of especially meat, chicken, pork²⁶ and saturated fat.²⁷

The logical conclusion is that the global epidemic of obesity and diabetes over the past 30 years is related to diets containing too much carbohydrate and too little fat and protein.^{25,27,28} But this possibility is of insufficient interest to be taught in medical schools. Instead the US Dietary Guidelines stress the need to increase the intake of 'healthy' carbohydrate and avoid 'artery-clogging saturated fats'.²⁷

I concluded that the cause of the global epidemic of obesity and diabetes is simple³ – both conditions occur in those who are genetically carbohydrate-resistant but who persist in eating the high-carbohydrate diet according to the US Dietary Guidelines. This interpretation is not novel – it was the standard teaching in most medical schools in Europe²⁹ and North America, but disappeared when the fallacious diet/heart hypothesis took hold in the 1970s.^{25,28}

But if obesity and diabetes are due to the overconsumption specifically of carbohydrates in those who are carbohydrate-resistant,^{3,16,25,28,29} then their prevention and cure require only that those who are the most severely affected eat a high-fat and -protein diet to which carbohydrates contribute less than 60 g per day.¹⁶ Yet as long as these conditions present massive commercial opportunities to the pharmaceutical and food industries, there will be no appetite for such a simple solution. Our sole recourse is to change the behaviours of those at risk, one meal at a time.

The evidence is tenuous for the related diet/heart hypothesis, which holds that a diet full of 'artery-clogging saturated fat' causes an elevation of blood lipid concentrations, thus promoting coronary atherosclerosis and ultimately heart attack.^{25,30} I argue that the evidence is essentially non-existent.³⁰

Opposing this is that coronary heart disease (CHD) is, like obesity and diabetes, an inflammatory disorder caused by abnormal carbohydrate metabolism in those eating a diet low in omega-3 polyunsaturated fats and high in trans fatty acids and omega-6 polyunsaturated fats.^{31,32} This seems logical since diabetes is, next to cigarette consumption, the strongest predictor of CHD risk. A single measure of carbohydrate resistance, blood HbA_{1c} concentration, is also a better predictor of CHD risk³³ than conventional blood lipid measurements.³⁰

Independent research shows that blood lipid measurements may be unrelated to CHD risk in men and women³⁴ and that women with serum cholesterol concentrations of 7 mmol/l are the healthiest. The Framingham study, which first established total serum cholesterol concentration as a risk factor for CHD,³⁵ revised their conclusions: 'After age 50 years there is no increased overall mortality with either high or low serum cholesterol levels'.³⁶ Instead, *falling* blood cholesterol levels after age 51 were associated with an 11% *increase* in overall mortality and a 14% *increased* death rate from heart attack for each 1 mg/dl per year drop in blood cholesterol concentrations. After age 50 years a low cholesterol concentration was associated with a reduced life expectancy. But how can the influence of a risk factor suddenly reverse on turning 50?

More damaging for the diet/heart theory was a finding that in the Framingham study: '... the more saturated fat one ate, the more cholesterol one ate, the more calories one ate, the lower the person's serum cholesterol ... the opposite of what the equations of Hegsted *et al.* (1965) and Keys *et al.* (1957) would predict ...' and that 'the people who ate the most cholesterol, ate the most saturated fat, ate the most calories, weighed the least, and were the most physically active'.³⁷

Indeed, the study that has produced the most profound reduction in recurrent events in those with established CHD, the Lyon Diet Heart Study, increased the dietary intake of omega-3 and reduced the consumption of omega-6 polyunsaturated fats. An editorial³⁸ noted that '... relatively simple dietary changes achieved greater reductions in risk of all-cause and coronary heart disease mortality ... than any of the cholesterol-lowering studies to date. This is emphasised by the finding that the unprecedented reduction in risk of CHD *was not associated with differences in total cholesterol levels between the control and experimental groups* [current author's emphasis] and that the survival curves showed a very early separation unlike what has been reported in the cholesterol reduction studies.'

Furthermore, this study 'indicates that there are other powerful risk factors within the realm of diet that must be considered if we are to achieve maximal dietary benefits in reducing this number 1 cause of mortality in the world today.'

The most recent meta-analysis concluded that 'there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of coronary heart disease or cardiovascular disease'³⁹ so that 'dietary efforts to improve the increasing burden of cardiovascular disease ... should primarily emphasise the limitation of refined carbohydrate intakes and the reduction in excess adiposity.'

Indeed, studies of the development of atherosclerosis in those below the age of 35 years⁴⁰ found that 'atherosclerosis in young adults is associated with the prediabetic or early diabetic state, as indicated by elevated glycohaemoglobin levels, and with obesity', so that 'the results provide hope that early detection and control of obesity and hyperglycaemia in young persons will reduce the risk of atherosclerotic disease in later life.'

Furthermore, '... obesity in adolescents and young adults, through mechanisms yet to be identified, accelerates the progression of atherosclerosis decades before clinical manifestations appear. Obesity is an important modifiable contributor to coronary atherosclerosis, particularly in young adult men, and efforts to control childhood obesity are justified for the long-range prevention of CHD and other chronic diseases. The increasing prevalence of obesity among young persons emphasises the need for obesity control efforts.'⁴¹

If obesity and diabetes are caused by the continued ingestion of high-carbohydrate diets by those who are carbohydrate-resistant, their prevention is simple. But since this conclusion undermines the diet/heart hypothesis of Keys and the use of statins in managing coronary atherosclerosis, it will not be taught.³⁰ The finding that statin use is associated with an increased risk for postmenopausal women developing diabetes⁴² will hopefully encourage a more open review of all the evidence, disproving the need for widespread and indiscriminate statin use.^{30,43}

Asked to support the adoption of the so-called 'prudent diet' to prevent heart disease, Dr Paul Dudley White, author of the classic cardiology text, *Heart Disease*, responded: 'See here, I began my practice as a cardiologist in 1921 and I never saw an MI (myocardial infarction) patient until 1928. Back in the MI free days before 1920, the fats were butter and lard and I think that we would all benefit from the kind of diet that we had at a time when no one had ever heard the word corn oil.'⁴⁴ This is in keeping with the evidence 50 years later that the closer North Americans have come to eating behaviours that correspond to the US Dietary Guidelines,^{26,27,44} so have they become increasingly less healthy with each passing generation.

The challenge

Louis Washkansky, the recipient of Professor Barnard's first heart transplant, had adult-onset diabetes that destroyed his heart. Had the aetiology of adult-onset diabetes been understood in the 1960s and had Washkansky been placed on a high-fat/high-protein diet and restricted carbohydrate intake once his state of carbohydrate resistance had been detected, he might not have required a heart transplant. In which case this article might never have been written.

But then, as now, prescribing a low-carbohydrate diet to prevent the complications of adult-onset diabetes in those resistant to carbohydrates, would not have been considered. Will the Faculty that gave the world the first human heart transplant be one of the first actively to challenge these two unproven entrenched dogmas?

If obesity, diabetes and coronary heart disease are caused by abnormalities of carbohydrate metabolism that are aggravated by prescribing diets high in carbohydrates and rich in trans- and omega-6 fats but deficient in omega-3 polyunsaturated fats, to those who are genetically predisposed because of carbohydrate resistance, then

those who disprove these currently accepted dogmas will do as much for the future of global health as have all the graduates of our Faculty over the past 100 years.

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