NEW MEDICAL SCHOOL WITH A CLEAR VISION

The stirring strains of the traditional Gaudeamus igitur surrounded the foundation students of Wollongong University’s new medical school as they filed into the University Hall for their welcoming ceremony. As proceedings unfolded, it soon became obvious that this fledgling Graduate School of Medicine (GSM) was embarking on a different journey to that taken by our established medical schools.

Significantly, the school has already forged strong partnerships with communities in the Illawarra and Shoalhaven districts, as was clear from the many community leaders present at the ceremony. The GSM’s primary goal is to graduate doctors committed to serving in regional, rural and remote Australia. In the words of the university’s Vice-Chancellor, the school’s model is designed “to address the shortage of [country] medical practitioners”. And this commitment explains why many of the inaugural students hail from regional and rural communities.

But it is its educational philosophy that really sets the GSM apart. It has shifted its teaching from tertiary care hospitals, with their emphasis on specialism, to health resources within the community, with their value of generalism. Almost 300 local doctors (more than half GPs) have honorary academic appointments with the GSM, and more than a third of its permanent academic staff members are from the local region. The focus of its research will be education.

A US academic recently observed: “Academic medicine is like a tripod, standing on three legs. One leg is patient care, one is research, and one is education. Over the course of the twentieth century, the emphasis placed on each of these missions has changed. In recent years, education has become the short leg of the tripod.”

The new medical school at UoW seeks to lengthen this leg. May its vision endure.

Martin B Van Der Weyden
**We need guidelines for diagnosis and treatment of polycystic ovary syndrome**

*Sabra M Lane*

**To the Editor:** The views expressed by Samaras et al underscore the call for national guidelines on diagnosing polycystic ovary syndrome (PCOS). Insulin resistance is the underlying metabolic disturbance in most patients with PCOS, but the disease is widely under-recognised.

Our association, the Polycystic Ovarian Syndrome Association of Australia (POSAA), hears weekly from individuals who have known for months, in some cases years, that they have a serious medical problem. Yet it is through their own persistence, not a thorough history-taking, that their condition is eventually diagnosed.

“Go home, lose weight” is the usual advice, but it is neither helpful nor appropriate. There is an urgent need among health care professionals and patients for greater understanding of fertility prospects, the risk of type 2 diabetes, and the need for lifelong exercise and permanent dietary changes. Even though women with PCOS cannot change their genetic makeup, they can take personal responsibility, which is more powerful than any drug in tackling this lifelong condition.

Our members tell us that many doctors regard PCOS as an issue of reproduction, with little regard to its metabolic characteristics. All women newly diagnosed with PCOS should be screened for insulin resistance or diabetes, as early identification allows them the best possible chance of living healthy, long lives.

As the incidence of PCOS and insulin resistance is rising, there should be national agreement on diagnosis and treatment. This should include an awareness campaign on what to look for, how to diagnose metabolic problems like PCOS and insulin resistance, and, crucially, how to treat them. Guides like the one given to POSAA by Kidson and Talbot and that published by the American Association of Clinical Endocrinologists should be endorsed for Australian doctors.

POSAA has agreement from the Royal Australian College of General Practitioners, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, and most state health ministers on the need for guidelines on diagnosing and treating PCOS. The MJA has copies of these letters. Yet, the federal government says “there is no specific funding allocation within the Department”, and Diabetes Australia says that current National Health and Medical Research Council (NHMRC) guidelines are appropriate. POSAA believes these guidelines are outdated.

Australia’s hidden epidemic of PCOS will only grow, matched by a ballooning financial burden on taxpayers, until governments, in partnership with the medical profession and groups like POSAA, work together to improve the health prospects of women with PCOS, and their families.

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**Insulin levels, insulin resistance and the use of metformin in polycystic ovary syndrome**

*Samantha K Hutchison, Sophia Zoungas and Helena J Teede*

**To the Editor:** We read with interest the recent article on insulin resistance, and we strongly support the argument that there is no current clinical utility to measuring fasting insulin levels. However, we are concerned about the statement that “otherwise well patients whom we see in practice are demanding (and receiving) metformin, or are being told they need it, particularly for polycystic ovary syndrome” (PCOS). Therapy in PCOS targets symptoms. Although Samaras et al imply that metformin is not required in “well patients”, the “well patient” is not defined. Most women with PCOS are, by definition, symptomatic, and most benefit from therapy.

We contend that, although measurement of insulin levels is not justified, insulin resistance is established in PCOS, and metformin is an effective treatment for women with PCOS. This contention is well supported in the literature. It is recognised that most women with PCOS have insulin resistance leading to hyperinsulinaemia and that insulin resistance plays a central aetiological role in the clinical manifestations of PCOS.

However, as outlined by Samaras et al, the insulin level is not an appropriate marker for insulin resistance (a challenging parameter to measure in routine clinical practice) and, consequently, insulin resistance is not included in the diagnostic criteria for PCOS.

Strategies to decrease insulin resistance have proven effective in studies where patients are selected based on clinical diagnostic criteria for PCOS, not insulin levels. Indeed, reducing insulin resistance with both lifestyle change and insulin sensitizers is emerging as a promising treatment strategy. Although not yet “approved” for treating PCOS in Australia, metformin is an effective treatment for anovulatory cycles and infertility, and induces a mild decline in hyperandrogenaemia. This is supported by a recent Cochrane review. Increasingly, metformin is recommended as a first- or second-line therapy in anovulatory infertility because, in contrast to conventional infertility therapies, it does not increase multiple pregnancy rates.

In summary, metformin treatment in PCOS is supported by a significant evidence base, but the use of metformin should be based on clinical indications, independent of an individual’s insulin levels.

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MATTERS ARISING

Insulin levels in polycystic ovary syndrome: a valuable tool
Warren J Kidson

TO THE EDITOR: As the person who introduced metformin as adjunctive therapy for polycystic ovary syndrome (PCOS) in Australia in 1996, and subsequently introduced measurement of insulin levels during glucose tolerance testing, I would like to respond to the article by Samaras et al.1

Samaras et al have included secondary causes of PCOS. However, as a result of incomplete maturation, stress, excessive exercise, or previous anorexia and bulimia, women may not respond to lifestyle change and will require more treatment. The authors have not mentioned that insulin resistance is frequently a component of PCOS, and often in their siblings and children. This may give an earlier warning of future metabolic and cardiovascular problems than conventional screening.

In summary, insulin levels are elevated in adolescence and early adulthood in women with PCOS, and often in their siblings and children. This gives an earlier warning of future metabolic and cardiovascular problems than conventional screening, at an age when people are less resistant to implementing lifestyle change, and giving a longer period for preventing pathology.

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Identifying insulin resistance is important to prevent development of glucose intolerance and the metabolic syndrome
Chee L Khoo

TO THE EDITOR: I congratulate Samaras et al for opening the debate on insulin levels, insulin resistance and the metabolic syndrome.1 It is true that, when measuring insulin levels, by the hyperinsulaemia-euglycaemic clamp, we define the lowest quartile of the population as insulin resistant. As insulin resistance is frequently a component of the metabolic syndrome, this method is already an underestimate. In 1999–2000, the prevalence of the metabolic syndrome among adults in the United States was 26.7%.2 The prevalence of the metabolic syndrome among participants of the Framingham Offspring Study and San Antonio Heart Study ranged from 21.3% to 32.8% during the early to mid 1990s.3 Various indices have been developed as surrogate markers of insulin resistance. HOMA-IR (homeostatic model approach—insulin resistance) is highly correlated with insulin resistance as measured by the euglycaemic clamp. HOMA-IR was useful in predicting type 2 diabetes and impaired glucose tolerance in the Mexico City Diabetes Study.4 Another study using HOMA-IR found that insulin resistance was positively associated with carotid plaque formation in subjects with normal fasting glucose and normal glucose tolerance. The associations remained significant even after adjusting for known atherogenic risk factors.5 Reducing insulin resistance reduces cardiovascular risk factors. The United Kingdom Prospective Diabetes Study reported that metformin is associated with a significant reduction in combined diabetes-related end points, diabetes-related deaths, all-cause deaths and myocardial infarction.6

By the time patients present to endocrinologists, they commonly already have many, if not all, of the elements of the metabolic syndrome. In primary care, we commonly see patients who only have one or two of those elements. Identifying insulin resistance early in at-risk patients is vital to prevent development of glucose intolerance as well as the various elements of the metabolic syndrome. Patients and their family doctors are interested in disease prevention and would like to know whether they are at risk of diabetes or the metabolic syndrome. As there is evidence

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2 Teede HJ, Hutchison SK, Zoungas S, Meyer C. Insulin resistance, the metabolic syndrome, diabetes, and cardiovascular disease risk in women with PCOS. Endocrine 2006; 30: 45-53.
which suggests that insulin sensitisers in conjunction with lifestyle modifications may be helpful in preventing progression to diabetes and reducing cardiovascular risk factors, their “demand” is not unjustified. Further, in obese, non-diabetic patients with insulin resistance, hyperinsulinaemia may act as a barrier to successful weight loss. Identifying insulin resistance in these patients is important, as metformin may have a role in assisting weight loss.

Primary prevention of diabetes and the metabolic syndrome is possible and achievable in the primary care setting.

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Insulin measurement is also inappropriate in paediatric obesity

Huy A Tran

TO THE EDITOR: I was pleased to read the article discouraging the measurement of insulin levels in the metabolic syndrome and obesity,1 as it concurs with my previous opinion.2 In parallel with the adult burden is the ever increasing paediatric obesity epidemic, which looms large across the world, with rates in Australia of up to 25%.3 This translates into a significant number of oral glucose tolerance tests being performed, often with measurement of insulin levels.

There is a distinct lack of evidence on the validity of this test in obese older children and adolescents in terms of defining cardiovascular and metabolic morbidity and mortality. The implementation and interpretation often stem from extrapolation of adult data.4 Furthermore, the administration of glucose to this age group is often impractical, as it is weight-based (1.75 g/kg, to a maximum dose of 75 g), and may induce morbidities such as nausea and vomiting, with subsequent failure to complete the test, multiple traumatic venepunctures, and unwarranted stress (both financially and emotionally) on the parents. Individual variations in gastric emptying and insulin secretion rate add to the poor accuracy and reproducibility of this so-called diagnostic test. If sufficient care is not taken, the analysis and processing of the insulin assay can give an incorrect result, and thus a low level can be misleading when clinical findings indicate otherwise. A high level merely confirms the syndrome where body mass indices and waist circumferences are equally valid measurements.5 Either way, this test cannot be recommended as routine, and management should be based on clinical features. Although not flawless, perhaps fasting plasma glucose levels are more appropriate as diagnostic tools, with oral glucose tolerance tests reserved for high-risk and atypical groups. These tests should be done without measuring insulin levels and with the previously mentioned confounders in mind.

Although it is recognised that insulin resistance is central to the disease clustering seen in the metabolic syndrome, unless the syndromal terms that bear the subtext “insulin” are renamed, insulin testing in clinical practice will continue unabated at a costly rate. In contrast to international bodies6,7 and this well-founded opinion,1 the National Health and Medical Research Council (NHMRC) still recommends insulin measurement,8 albeit in selected circumstances.

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The cost of measuring insulin levels can be justified

Allen E Gale

TO THE EDITOR: Samaras et al1 state that individuals at risk of diabetes and atherosclerotic cardiac disease can be identified simply and inexpensively by history-taking, physical examination, and very basic investigations. However, insulin resistance and beta cell failure are the hidden causes, and predate the development of overt diabetes by more than a decade.2 Doctors should help patients to understand that the progression of these conditions can be halted by significant changes to lifestyle.3 These will reduce the need for expensive medications, and in some cases even obviate their use.

As most obese individuals have battled unsuccessfully to lose weight, and non-obese individuals may also be insulin resistant,4 an assessment of glucose and insulin responses in an oral glucose tolerance test should assist the physician in developing a treatment plan. Unfortunately, few clinicians take the time to explain the difficult concept of insulin resistance.

Until the recent Enhanced Primary Care program, few individuals were able to afford the advice of dietitians or an exercise physiologist. Most clinicians have given up attempts to motivate patients to exercise regularly and lose weight, and many take the easy course of prescribing medications. Although Reaven first described insulin resistance as the basic pathophysiology of type 2 diabetes in 1988,5 it is only since the advent of the glitazones that clinicians have embraced the concept. Furthermore, not one person with type 2 diabetes that I have encountered has heard of the term insulin resistance. An explanation of insulin resistance assumes new meaning when illustrated with a patient’s own glucose and insulin responses after a glucose drink or their usual breakfast.

MATTERS ARISING

5 Reaven GM. The metabolic syndrome: is this diagnosis necessary? Am J Clin Nutr 2006; 83: 1237-1247.
TO THE EDITOR: The authors of the article on insulin resistance challenge users of serum insulin levels to demonstrate benefit in clinical practice.

A picture is worth a thousand words

Chris Strakosch

TO THE EDITOR: The authors of the article on insulin resistance challenge users of serum insulin levels to demonstrate benefit in clinical practice.

A typical glucose tolerance test result showing the insulin response “off the page”

Dots = measured glucose levels; dotted lines = glucose normal range. Crosses = measured insulin levels; shaded area = insulin normal range.

Insulin levels in insulin resistance: phantom of the metabolic opera?

Katherine Samaras, Timothy A Welborn, Aidan McElduff, Joseph Proietto, Stephen M Twigg, Paul Zimmet and Lesley V Campbell

IN REPLY: We are pleased that our article stimulated debate regarding the inappropriate measurement of insulin levels in clinical practice.

Lane, representing the Polycystic Ovarian Syndrome Association of Australia (POSAA), presents an impassioned plea for more effective diagnosis and treatment of polycystic ovary syndrome (PCOS). Her concerns focus on the general lack of knowledge about diagnostic criteria and the condition itself. We support the wider recognition of this condition, the greatest cause of infertility in this country. However, PCOS cannot be diagnosed or measured in any way by insulin levels, even though about 80% of patients are insulin resistant. Lane also calls for Australian guidelines for diagnosis of PCOS; these are not necessary, as simple, widely accepted international guidelines exist. As pointed out by Hutchinson et al, estimates of insulin resistance are not required for diagnosis of PCOS.

PCOS is common and costly, both in absolute fiscal terms (eg, in-vitro fertilisation) and in quality of life and other, inestimable “human” terms. We recognise the great suffering of women with PCOS, and the heartbreaking difficulties of infertility, with its intrusive and expensive management. These factors make these women vulnerable as consumers, so it is important to inform POSAA and other consumer groups of useless measures that have no evidence base in diagnosis and treatment. Rightly, Lane expects medical practitioners and departments of health to agree on diagnostic guidelines for PCOS, and Hutchinson et al anticipate the approval of metformin therapy in PCOS with clinical indications such as anovulatory infertility. The role of metformin in treating PCOS is not in dispute here. However, independent of symptoms or signs of PCOS, prescribing metformin after “diagnosis” of insulin resistance based on insulin levels is negligent. We agree unanimously with Hutchinson et al that “use of metformin should be based on clinical indications”.

Kidson agrees that insulin measures are unreliable. His referenced comments highlight that insulin measures only have an...
Tran points to the dominant role of the obesity epidemic, the overwhelmingly large elephant in the room we have thus far ignored. Obesity causes (and worsens) insulin resistance, and causes diabetes, heart disease, stroke and some cancers. With 60% of the adult Australian population now overweight or obese, we can expect a greater frequency of insulin resistance in the community. Tran presents a convincing, well researched argument against measuring insulin levels in either fasting or during an oral glucose tolerance test. Measures of central abdominal obesity (eg, waist circumference) have been shown in long-term studies to be the best predictors of heart disease, diabetes, cancer and all-cause mortality.

Any strategy that assists obese people to lose weight will reduce insulin resistance and components of the metabolic syndrome, particularly diabetes and heart disease. Motivating patients in lifestyle change is a difficult and perpetual challenge for the clinician. Nevertheless, we find it astonishing that clinicians use insulin levels to enhance motivation, as suggested by Strakosch. This is truly invoking phantoms. We encourage all clinicians in our difficult task of counselling and motivating lifestyle change. The creation of a facilitating environment to offset the Australian obesity and diabetes epidemic is a high political priority.

We also thank Gale for emphasising the importance of lifestyle management in diabetes and related pre-diabetes conditions. However, his comment that the cost of measuring insulin levels can be justified is not supported by any evidence, and leads to a question as to who should bear the cost.

Who is bearing the cost of measuring insulin levels? This burden falls mainly on the Health Insurance Commission (HIC). If patients were made to bear the cost, they might demand greater clinician scrutiny of its validity. Is it appropriate for the Australian taxpayer and the precious medical budget to fund an unvalidated and unreliably poor estimate of an entity that, by best practice, does not need to be measured? We acknowledge that insulin levels have a role in epidemiology and research — but only there, and the HIC has very clear guidelines that it is inappropriate to fund research through Medicare.

**Competing interests:** Most of the authors have received ad-hoc honoraria for delivering lectures on their research or clinical interests at general practitioner or specialist educational meetings; some have also received travel assistance to attend international scientific meetings.

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Evidence base in epidemiology. Again, we invite evidence for utility of measuring insulin levels in clinical practice, if it “can ever be presented”. "Tran points to the dominant role of the obesity epidemic, the overwhelmingly large elephant in the room we have thus far ignored. Obesity causes (and worsens) insulin resistance, and causes diabetes, heart disease, stroke and some cancers. With 60% of the adult Australian population now overweight or obese, we can expect a greater frequency of insulin resistance in the community. Tran presents a convincing, well researched argument against measuring insulin levels in either fasting or during an oral glucose tolerance test. Measures of central abdominal obesity (eg, waist circumference) have been shown in long-term studies to be the best predictors of heart disease, diabetes, cancer and all-cause mortality.

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