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**Australasian Diabetes in Pregnancy WEBSITE**

Information about the society can be found at: [www.adips.org](http://www.adips.org)

Information about the International Association of the Diabetes and Pregnancy Study Groups can be found at: [http://www.iadpsg.org](http://www.iadpsg.org) with links to ADIPS and other regional study groups.

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*Capri, Italy*
Hello everyone,

The year is zipping by quickly and I need to get this to press so that you all have plenty of time to plan your trip to ADIPS this year in AUGUST, held again in Adelaide, as we are meeting to overlap with the ADS and ADEA conferences. An exciting programme is planned – please encourage your young team members to come along. I have included dates and web reference for registration and abstract submission under “dates for your diary” in the newsletter.

There have been several interesting conferences already this year. I was lucky enough to go to India in February: firstly, to the Asia-Oceanic Conference on Obesity in Mumbai, which was unfortunately down on numbers after the bombings a few months earlier.

The conference included a surgical thread and by the time I came to the end of the day that I attended, I decided that we just need to trick the gut hormones by whatever intervention possible – of which surgery, or even a “sleeve” in the gut may be a good therapeutic option and obesity and diabetes will become historical terms…. but, maybe not just yet. I then went on to Chennai for a day to the “DIPSI” (Diabetes in Pregnancy Society of India) conference, quite a large and lively meeting. I have written a paragraph for the Newsletter highlighting some interesting points I gleaned from the abstract book.

That night, we were off to Pune, where Chittaranjan Yajnik is from. I spent a fascinating day in his unit and talked to the obstetricians and endocrinologists about MiG. For those of you who have never been to India it is very interesting and stimulates all the senses. I thought I was observing their life but I realised after a day that many people, especially children, were busy observing me – and finding me very amusing! It seems my short silver (not grey) hair is a rather peculiar sight!

In March, the 5th International Symposium on Diabetes and pregnancy was held in Sorrento, Italy. The meeting was attended by over 1200 delegates with a decent smattering from Australia and New Zealand. India came to Sorrento in that Chittaranjan Yajnik gave some exciting talks about nutrition, programming and body composition in the Asian-Indian population. Wah Cheung has summarised the themes from Ranjan’s talks.

One of our members, Ruth Hughes, went to the Third International Congress on Prediabetes and Metabolic Syndrome in Nice, France. She managed to avoid too many distractions and did attend the conference, as you will read. I also happen to know that she had a great day sightseeing at the end and did not realise until she was trying to check in at the airport that she had missed her flight by 24 hours! Still, they managed to pop her on a flight and all ended well.

I wanted to include draft recommendations about criteria for diagnosing GDM based on the HAPO data, but the document is still being drafted by the writing committee and I would probably be shot at dawn if I published anything confidential. I can say that there has been a lot of agreement between members of the international committee about how we should test for GDM and what the criteria for diagnosis should be, but there are a few areas that have not been completely resolved. Also, the committee is trying to make recommendations about...

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Editor’s Comment
screening for undiagnosed type 2 diabetes in early pregnancy for which there are no good data to help guide the discussions. Hopefully this will not delay the rest of the document. Jeff Flack has written a piece about implications for our services if the criteria are changed, providing ongoing food for thought. He did discuss this at the ADIPS conference last year, but I thought it was an important issue to highlight, as we do really need to think ahead about our models of care as our numbers increase even in the absence of changes in diagnostic criteria.

Also, I am hoping that we will soon see an updated ADIPS recommendation about oral agents for the treatment of GDM, specifically metformin. I know this is being written and it is likely to be circumspect until we see follow up data of MiG offspring (TOFU).

The two year old children of MiG have just about finished their assessments, so the TOFU team will be working during the second half of the year to write a manuscript reporting these outcomes. Interestingly, in Sorrento there was a debate about oral agents, but the debate centred on the use of glibenclamide and it felt like I was asked to discuss metformin almost as an aside. I am pleased to report however, there was a lot of interest in metformin and clinicians are really starting to think about its role. There were also two posters about metformin use in women with GDM and both were favourable for metformin, although numbers were smaller than the MiG trial.

I am hoping that in the next Newsletter we will report on our ADIPS conference, provide clearer answers from HAPO and provide some commentary about oral agents. Please do send me ideas, contributions, photos.

Janet Rowan, Editor
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Dates For Your Diary

The ADIPS annual meeting follows the ADS (Australian Diabetes Society) / ADEA (Australian Diabete Educators Association) meeting in Adelaide. We have a combined session with them at the Convention centre on Friday the 28th in the morning...

ADS/ADEA:
26th-28th August 2009, Adelaide Convention Centre

ADIPS:
28-30th August 2009, Novotel Barossa Valley Resort (buses will transport us from the Convention Centre on the Friday afternoon after a joint session with ADS, ESA and then back on Sunday I understand to the airport or town as options).

Find out information, register and submit abstracts for the ADIPS conference either through our ADIPS website or direct to www.asnevents.net.au/adips. Earlybird registration closes June 19th, and online abstract submission closes July 10th.

There are preliminary programme details on the website and we are looking forward to having professor David Sacks as our guest speaker. He is an obstetrician and gynaecologist and MFM specialist from Kaiser Foundation Hospital, Bellflower, California.

EASD:
European Association for Study of Diabetes:
27th Sept-01 Oct, 2009 Vienna, Austria
www.easd2009.com

DoHaD:
Developmental origins of Health and Disease.
November 19-22nd Sheraton Convention Centre, Santiago, Chile
www.dohadsoc.org
I was only able to attend one day of this meeting, but was given the abstract book to take home. The topics I heard discussed on the day I attended were similar to ones we hear at our annual meetings— all interesting, but no major tips for ADIPS readers.

In the abstract book I was interested to read about a study performed in 350 Asian-Indian women that were recruited during the first trimester of pregnancy. Women with known glucose intolerance, previous GDM, more than one fetus or taking metformin or steroids were excluded.

The women were asked to perform a 100g 3 hour oral glucose tolerance test (OGTT) at < 13 weeks' gestation to see how many women had GDM by Carpenter and Coustan criteria (at least two of the following: fasting ≥ 5.3mmol/l, 1-hr ≥ 10.0mmol/l, 2-hr ≥ 8.6mmol/l, 3-hr ≥ 7.8mmol/l). Women who were diagnosed with GDM were treated and the remaining women had a repeat 100g OGTT between 24-28 weeks’.

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In this study, 8.1% of women were diagnosed with GDM before 13 weeks. Of the remaining women, 7.4% were diagnosed with GDM at 24-28 weeks. The overall prevalence in this Asian-Indian population was 15.8%. There were some differences in baseline characteristics in women who were diagnosed in the first trimester compared with the rest of the group in that they were older with a higher BMI (but no difference in rates of obesity) and they had more previous poor obstetric outcomes.

This abstract was from E Grewal, S Kansra, R Khadgawat, G Kachhawa, AC Ammini, A Kriplani, M Ashad, N Aggarwal from the All India Institute of medical Sciences, Delhi.

Another abstract talked about women with an elevated 75g glucose challenge test (> 7.8mmol/l) and then a diagnosis of GDM by 100g OGTT (Carpenter and Coustan, I think).

These women undertook a seven value sugar profile for a day prior to any intervention. Women who had a “normal” profile (not detailed) were monitored clinically for macrosomia and polyhydramnios and had a sugar profile every 2-3 weeks. If there were clinical concerns or more than one elevated glucose level was seen when the profile was performed women were excluded from the study group and diet therapy was started.

In the study group there were no perinatal losses, birth weights were between 2.8-3.1kg and the caesarean rate was 17%. Unfortunately there are no numbers in the abstract, but these data may be interesting to look out for if published. The abstract was from S Tyagi, YM Mala, R Tripathi, Maulana Azad Medical College, Delhi.

Janet Rowan
Physician, Auckland
**Folate, B12 and Pregnancy**

*(From the 5th International Symposium on Diabetes and Pregnancy, Sorrento, Italy)*

Professor Chittaranjan Yajnik gave two very eloquently presented talks relating to folate, vitamin B12 and pregnancy. The first was a discussion of the effect of maternal nutrition on the offspring, with particular reference to fetal programming.

The second was in a debate on the merits of folate supplementation in pregnancy. The ADIPS members who attended the ADIPS Annual Scientific Meeting in Akaroa will remember Chittaranjan Yajnik as our international guest speaker at that conference. At that meeting, he informed us of the Pune Maternal Nutrition Study (PMNS). In the PMNS he established a cohort of women in the Pune region of India, whom he collected data on before, during and after pregnancy. Additionally, he has been able to follow-up over 700 offspring, now aged 12 years.

In these studies, an enormous amount of data about diet during pregnancy and maternal blood samples were collected. Subsequent analyses have highlighted the importance of a balanced micronutrient intake. In the PMNS cohort, low vitamin B12 levels were found in two thirds of the mothers. On the other hand, folate deficiency was extremely rare. This is probably because many of the women were lacto-vegetarian, and even those who were not, ate little meat. The B12 deficiency contributed significantly to hyperhomocysteinaemia. Both hyperhomocysteinaemia and lower maternal folate levels were associated with small babies. When the children were followed up, those whose mothers had low B12 and high folate were the most insulin resistant, as determined by HOMA-R (and maternal hyperglycemia worsens the situation).

These findings suggest that folate supplementation can be detrimental in the presence of vitamin B12 deficiency, particularly if the population is folate replete. The implication is that this may be a mechanism of fetal programming for a diabetes phenotype, and contribute further to the diabetes epidemic in India.

The relevance to us in ADIPS is that we recommend high dose folate during pregnancy planning and in the first trimester of pregnancy to our patients with pre-existing diabetes, without necessarily considering the woman’s B12 status. Vitamin B12 status really should be evaluated in women who are vegetarian, particularly common amongst Indians, and also in those who have been receiving Metformin, and replaced (orally) if necessary.

*N Wah Cheung*  
Clinical Associate Professor, University of Sydney, Staff Specialist Endocrinologist, Westmead Hospital

(Editors note: for further information about this topic, a recent review written by Dr Yajnik is worth reading (and his previous papers) Yajnik C. Nutrient-mediated teratogenesis and fuel-mediated teratogenesis: two pathways of intrauterine programming of diabetes. Int J Gynecol Obstet 2009 ar;104 Suppl 1:S27-31. This supplement also contains a number of other articles about diabetes in pregnancy)
Third International Congress on Prediabetes and the Metabolic Syndrome.

I skipped over to France from the EDIP symposium in Sorrento to take a chance on this meeting. It was great! Not only was Nice a lovely place to visit, with one Euro bus tickets taking you to nearby walled villages and the wealth of Monaco, but the meeting was well organised and had a number of excellent and enthusiastic key speakers. There were two daily plenary sessions intertwined with a choice of four parallel sessions, all hard to choose from.

A number of drug-company sponsored satellite symposia kicked off the meeting. There was a session on the incretins, particularly GLP-1 which has an important role in diabetes. The incretins are gut hormones that are secreted in response to feeding. GLP-1 improves beta-cell mass and function, as well as promoting weight loss via decreasing appetite and increasing satiety. Patients with type 2 diabetes have both impaired GLP-1 secretion and reduced beta-cell responsiveness to GLP-1, which (luckily for the drug companies) is overcome with large amounts of exogenous GLP-1. Interestingly, GLP-1 was found to be reduced in women with gestational diabetes (GDM), but the levels returned to normal postpartum. We were not told what happens to GLP-1 secretion in normal pregnancy, or of any potential therapeutic benefit of GLP-1 in the management of GDM, but it is interesting to speculate that medications targeting GLP-1 secretion may be important with respect to future management options.

He concluded that the genetics of polygenetic obesity supports obesity rather than insulin resistance as the aetiologic agent of in all components of metabolic syndrome.

Native GLP1 is rapidly degraded by DPP-4 and cleared by the kidneys, and a number of therapeutic agents have been developed including GLP-1 receptor agonists (Liraglutide and Exanatide) and DPP-4 inhibitors sitagliptin. The main advantages of the GLP-1 mimetics over the DPP-4 inhibitors are that they significantly reduce food intake, result in greater weight loss, and result in slightly improved glycaemic control with fewer hypoglycaemic episodes and less nausea. One disadvantage is that GLP-I mimetics need to be given by subcutaneous injections rather than orally. Cardiologists may also be interested in GLP-1 due to its protective role on the cardiovascular system, reducing the inflammatory markers PAI-1 and CRP, and also BNP and triglycerides. In animal studies GLP-1 infusions decrease infarct size and improve survival post myocardial infarction.

Plenary sessions included discussions on metabolic syndrome, inflammation and abdominal obesity. The current hot topic ‘Should we redefine measurements of blood glucose control and categories of dysglycaemia?’ was debated with some favouring a move away from the glucose tolerance test towards markers of longer-term glycaemia such as the HbA1c, and others favouring a multifactorial risk-score approach for diagnosis.
Dr Sigal, Canada, presented his own data on the role of physical exercise on glycaemic control in type 2 diabetes. In a randomised trial he showed that a combination of aerobic and resistance training was better than either alone at producing more weight loss despite a gain in fat free mass, and a greater reduction in HbA1c.

**Highlights from the conference included:**

Andrew Hattersley, Exeter, UK, who asked the question ‘Is there a common genetic link between metabolic syndrome, type 2 diabetes and cardiovascular disease?’ since they share multiple common risk factors. After a genome wide search no genetic link was found, in particular no common genetic variants were robustly associated with insulin resistance. He concluded that the genetics of polygenetic obesity supports obesity rather than insulin resistance as the aetiologic agent of in all components of metabolic syndrome.

Dr M Hanson, Southampton, UK, who gave an excellent talk on ‘Developmental plasticity and human disease’, which all relates to “Developmental origins of Health and Disease (DoHaD).” he described how the mother’s body influences the child’s gene expression (epigenetics) and development from the moment of conception ‘teaching’ the baby about the environment it will be born in. But what if the postnatal world is different eg a dietary imbalance?

The child may not be programmed to deal with energy dense food, for example and be more susceptible to as the development of obesity, diabetes and cardiovascular disease as he or she ages. An interesting point was that an unhealthy maternal diet (high in sugar and fat) was shown to change fetal blood flow, with less blood through the ductus venosus shunt and more through the liver, and was associated with a fatter baby independent of the mother’s slenderness.

Finally, there was an excellent plenary session on soft drinks! B. Popkin, Professor of Nutrition, Chapel Hill, USA, described the global dimensions of sugary beverages and programmatic and policy solutions. The obesity epidemic has paralleled the global explosion of soft drinks since the 1980’s, and data suggest that 1/3 – 2/3rds of the observed weight gain in populations could be secondary to calories from beverages. Apparently humans have only consumed calorific beverages in the last 100 years, moving away from water and milk to soft and alcoholic drinks. Even the Romans diluted their wine 3-4:1 with water. A major problem with this is that when humans drink calorific beverages they don’t compensate by reducing food intake. Obesity is such a problem in Mexico that the government is in the process of banning full and half-fat milk, and all soft drinks (fizzy and fruit juice) from all government programmes. There is also a push for beverage taxes in the US. “Regulation and taxation as per cigarettes is the only way to curb the soft drink epidemic and will have a major effect on adiposity and cancers.”

Dr Bray, Baton Rouge, USA, concluded the session with some more sobering evidence on the dangers of fructose in our beverages. Fructose increases thermogenesis more than glucose, and increases glucose oxidation and may actually contribute to hunger and increased energy intake. Fructose, more than glucose, elevates triglyceride levels and diastolic blood pressure. Even more worrisome a randomised trial (Stanhope et al JCI 2009 in press) showed that visceral fat but not body weight was increased by sucrose, but not glucose, consumed in beverages - yet another reason to advise pregnant women with diabetes against drinking fruit juice.

Ruth Hughes, Obstetric Physician, Christchurch, NZ
It is nearly 2 years since the presentation of the HAPO study findings at the ADA, and now over 12 months since the publication of the outcomes1. It was anticipated that the HAPO data would be used to redefine GDM diagnostic criteria, yet despite several international meetings, no decision or agreement has as yet been reached on how to implement the findings. It has been suggested in particular that the fasting BGL cut-off will be lowered, but it is unclear what 1hr and/or 2hr cut-offs will be recommended. At the 2008 SOMANZ / ADIPS meeting in Adelaide we presented our data modeling likely implications on workload2.

We found that a rise in the 2hr cut-off (from Australian criteria of 8.0mmol/l) would ameliorate the increasing numbers of women diagnosed with GDM resulting from a drop in the FBGL cut-off alone. If, however, the 2 hour remained unchanged in Australia and the fasting was reduced, this led to significant changes in rates of GDM. (Editor: see attached abstract) Our conclusions, based on predictions of workload increase from a reduced FBGL cut-off only were:

- It is predicted that multidisciplinary teams involved in the management of newly diagnosed GDM will find it difficult to cope with an increase in the number of patients of this magnitude, and
- Even more resources and/or a redirection of efforts to manage these women, including appropriate follow-up, will be required if we are to address this significant condition and decrease the later development of type 2 diabetes in this at-risk group.

We were disappointed to read in the last Newsletter that one interpretation of this presentation was that we were calling for circumspection from the HAPO investigators in determining diagnostic cut-offs. This was not the case and a key point in the presentation was that we are NOT pushing an agenda that says ‘you can’t change the criteria because that will increase our workload too much’. The discussion in Adelaide at the ADIPS 2008 meeting was dominated by how we could cope, and there was no universal agreement in regards to what we should do.

If [when] there are changes – we may need to change the way we currently structure our services to manage GDM – substantially in many units – in order to cope with the likely increased numbers of referrals we would be asked to see.
How could we approach this?

One suggestion is to stratify risk after diagnosis. HAPO found no threshold effect and that a continuous and linear association existed between maternal glucose level [particularly FBGl], and adverse outcome measures. Those women diagnosed at the lower end of the ‘new’ diagnostic range may be expected to be at ‘lower risk’ and their management ‘may’ be able to be varied by the introduction of ‘less stringent’ management practices – perhaps less frequent clinic review – phone contact only etc.

There would need to be systems in place however to identify and manage cases with inappropriate progress [high BGLs, large baby etc]. We will need to assess whether women whose GTT levels are at the lower end of the range continue to track at lower levels of glycaemia and risk than those whose OGTTs show higher BGLs. This may not be the case, which would not be so surprising given the low reproducibility of the OGTT.

One strategy could be to involve Midwives more in managing these ‘lower risk’ women, providing referral pathways back should there be unacceptable BGL results. There would need to be a willingness from Midwives to take on this additional role and ongoing educational initiatives to develop and assess guidelines and protocols in order to achieve this as an option. If not already doing so, one option would be for services to implement group rather than one-to-one education of women.

Alternatively, if we need to deliver the current level of services that we do in terms of providing regular diet review/support and review of their meter memory and BGL records, it may be that nothing short of enhanced funding and staffing will be needed if HAPO is showing that even mild levels of hyperglycaemia are associated with adverse outcomes and likely higher rates of abnormal glucose tolerance & obesity in future generations.

Services already stretched by increasing numbers diagnosed by current criteria, may have already implemented some or all of the above, or indeed implemented other ‘novel’ strategies or programs. The purpose of this article is to stimulate further consideration and discussion of how we can provide appropriate services to women with GDM in order to achieve appropriate outcomes for mothers and their babies.


2. Impact On Workload If The HAPO Study Findings Result In Changes To GDM Diagnostic BGL Cut-Off Levels. S. Ho, G.P. Ross, M. Ha, J.R. Flack*. Department of Diabetes and Endocrinology, Bankstown Hospital, NSW.

It is predicted that multidisciplinary teams involved in the management of newly diagnosed GDM will find it difficult to cope with an increase in the number of patients of this magnitude.