

She made an uneventful postoperative recovery. Conclusion: LAGB accounts for only 5.5% of all bariatric surgeries. This has largely been due to reported removal rates of up to 40% after 7 years secondary to complications. Only four other case reports of cecal volvulus from LAGB have been described. Surgeons should have a high index of suspicion of a volvulus in a patient with an acute abdomen as a late complication of LAGB.

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263

### Persistent leptin signalling in the arcuate nucleus reduces insulin's capacity to suppress hepatic glucose production in obese mice



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Since the discovery of leptin 23 years ago, a major challenge to weight loss strategies in obesity is leptin resistance. The lack of response to exogenous leptin administration in obesity is not only an obstacle to energy homeostasis regulation, but it could also be involved in the type 2 diabetic phenotype associated with obesity.

Our previous work *in vivo* and *ex vivo* with diet-induced obese mice (DIO) suggested that contrary to expectations, leptin signalling remains functional and is permanently activated in arcuate nucleus of the hypothalamus (ARH) neurons of DIO mice. This state of constant response to endogenous leptin underpins the lack of response to exogenous leptin. The obese phenotype of DIO mice is also associated to glucose intolerance, caused by a decreased sensitivity to insulin. The immunohistochemistry study of combined leptin and insulin signalling leads us to conclude that there is a common pool of ARH neurons responding to both leptin and insulin.

We then hypothesized that the constant activation of LepRb-neurons in the ARH of DIO mice could prevent insulin signalling in these neurons, leading to impaired glucose homeostasis and type 2 diabetes.

Accordingly, immunohistochemistry and hyperinsulinemic euglycemic clamps experiments demonstrated that antagonizing central leptin signalling in DIO mice restores hypothalamic insulin signalling and decreases hepatic glucose production. Using icv injection of inhibitors and ARH specific gene deletion, we identified protein phosphatase 1B (PTP1B) as the main mechanism by which the constant leptin signalling inhibits insulin response in ARH neurons of DIO mice.

Altogether our results bring new insights in obesity-linked central insulin resistance and open a potential new path of therapeutic strategy to treat type 2 diabetes in obese patients.

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264

### Crosstalk between hypothalamic leptin and insulin signalling in obesity



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Obesity is characterised by increased adiposity, high leptin levels, and leptin resistance. Plasma leptin concentration is positively correlated with fat mass. Fasting decreases body fat and consequently decreases leptin levels. Obesity is a risk factor for type 2 diabetes mellitus (T2DM). T2DM is characterised by increased fasting glycaemia and impaired glucose tolerance. Insulin resistance is a common feature between obesity and T2DM. Leptin and insulin act on the same neuronal population within the arcuate nucleus of the hypothalamus (ARH). Our previous work demonstrated that Diet-induced obese (DIO) mice show no response to insulin, but still demonstrate leptin signalling in the ARH. Pharmacological blockade of leptin signalling in the CNS restores insulin signalling in DIO mice, thereby improving glucose homeostasis. However, utilising fasting to decrease leptin level and exert a physiological rescue of insulin signalling has not been investigated yet. We hypothesised that decreasing endogenous leptin level using a 48-hour fasting could reduce leptin response in the ARH and promote the restoration of insulin signalling and glucose tolerance in DIO mice. Mice are fed with chow diet or high-fat diet for 20 weeks, followed by a baseline glucose tolerance test (GTT). After a two-week recovery, the DIO mice will then be divided into two groups: 'DIO fed' mice, fed *ad libitum*, or 'DIO F48' mice, fasted for 48 h prior to the final GTT undergone by all mice. Following the final GTT, mice received either saline or insulin for histological signalling studies. Brain slices will be immuno-stained for phosphorylated signal transducer and activator of transcription-3 (pSTAT3) and phosphorylated protein kinase-B (pAkt). pSTAT3/pAkt co-localisation is used a marker of leptin receptor activation, while pAkt-alone a marker of insulin action. This will determine whether reducing leptin level will decrease endogenous leptin signalling and possibly restore insulin action in the ARH of DIO mice.

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300

### Descriptive analysis of adult patients referred to the nepean family obesity service in the first six months of service operation



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The Nepean Blue Mountains Family Obesity Service (NFOS) was set up in 2016 to deliver multidisciplinary healthcare to those with obesity across the lifespan. This file audit was carried out to identify the demographics, clinical characteristics and basic health outcomes of adult patients referred to the NFOS in the first six months of operation. Of the 83 patients referred to NFOS, 71 were included in the audit (8 patients did not attend any appointments, 2 attended the initial group session only, 1 was outside our local health district

and 1 was excluded due to missing data). At the time of audit, 20 out of 71 patients were lost to follow up (28%).

There were 53 female and 18 male patients that attended, with an average age of 50.5 years (range 18–73). Referrals originated from GPs ( $n=65$ ), endocrinologists ( $n=4$ ) and cardiologists ( $n=2$ ). Ethnicity included Caucasian ( $n=64$ ), Aboriginal ( $n=3$ ), Indian ( $n=2$ ), Fijian-Indian ( $n=1$ ) and Peruvian ( $n=1$ ). The average weight of the patients was 143.1 kg (range 95.4–288.8), average height was 1.678 m (range 1.511–1.912), average BMI was 50.7 kg/m<sup>2</sup> (range 34.7–97.6) and average waist circumference was 145.3 cm (range 116–276). Some of the most common co-morbidities in these patients were diabetes mellitus, hypertension, hyperlipidaemia, sleep disordered breathing and chronic pain.

All patients received multidisciplinary care with dietitian, physiotherapist, clinical psychologist, nursing and medical appointments. VLED was initiated in 16 patients. Any form of weight-modulating pharmacotherapy was initiated in 35 patients, including 23 on metformin, 18 on GLP-1 analogues, 1 on phentermine and 1 on topiramate, and 11 patients were identified as surgical candidates.

The adult arm of our service has seen patients with a wide spectrum of obesity, medical co-morbidity and treatment suitability. An ongoing challenge includes balancing weight loss interventions with management of complex medical co-morbidities and a high rate of patient attrition from clinic.

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301

### Efficacy of very low-energy diets for weight loss: a systematic review of intervention studies in children and adolescents with obesity

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**Objectives:** Very Low-Energy Diets (VLEDs) lead to rapid weight loss in adults. This systematic review aimed to evaluate the efficacy and safety of VLEDs for weight loss in children and adolescents with obesity.

**Methods:** A systematic literature search of six health and medical databases was conducted in November 2017. Eligible studies were in English, studied a VLED providing  $\leq 800$  kcal/day (3350 kJ) or  $<50\%$  daily estimated energy requirements in children and adolescents ( $\leq 18$ -years) with obesity and reported at least one weight-related outcome. Quality appraisal was conducted using The Academy of Nutrition and Dietetics quality criteria checklist and study data extracted. Meta-analysis was performed using Comprehensive Meta-Analysis software.

**Results:** Twenty-four studies met inclusion criteria and were included (16 pre-post studies, 4 non-randomised comparison studies, 2 randomised controlled trials, 2 chart reviews). The VLED intervention duration ranged from 3–24 weeks. Meta-analysis of 20 studies reporting the effect of VLED intervention on weight outcomes indicated a mean 8.1 kg weight loss (95% confidence interval [CI]: 7.1 to 9.0 kg,  $p < 0.001$ ) post-intervention. Adolescent-only studies (10–18 years) had greater weight loss compared to

child and adolescent studies (17.7 kg, CI: 9.9 to 25.6 kg,  $p < 0.001$ ,  $n=4$  versus 7.9 kg, CI: 7.0 to 8.9 kg,  $p < 0.001$ ,  $n=16$ ). Meta-analysis of seven studies reporting weight at follow-up (up to 14.5 months from baseline) indicated mean 5.2 kg weight loss (CI: 2.7 to 7.7 kg,  $p < 0.001$ ) from baseline. Only 12 studies reported intervention side-effects, five reported no adverse effects and seven reported mild side effects, including fatigue, hunger, nausea.

**Conclusions:** Current evidence suggests VLEDs are safe and effective for treating children and adolescents with obesity. Compared with traditional dietary interventions, VLEDs appear to be more effective for weight loss, although further studies in children are warranted. Future studies should determine strategies for maintaining weight loss following a VLED intervention and comprehensively assess adverse effects associated with VLED adherence.

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302

### Clinical Obesity Services in Public Hospitals (COSiPH) in Australia: a position statement based on expert consensus

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