

# the medicine cabinet: Obesity – Problem of Number and Size...

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Childhood obesity is one of the most serious public health challenges of the 21st century.<sup>1</sup> Excess body weight is the sixth most important risk factor contributing to the overall burden of disease worldwide. Obesity is a preventable disease and the incidence of obesity has doubled since 1980<sup>2</sup>. Nearly 43 million children under the age of five were overweight in 2010 with majority in developing countries. In 1995, 19-23% of Australian children and adolescents were overweight or obese. Between 1985 and 1995 the prevalence of being overweight in this age group had almost doubled and that of obesity had more than tripled<sup>3</sup>.

The cause of obesity is multifactorial but results in the main from a chronic imbalance between energy intake and energy expenditure<sup>9</sup>. The widely held belief is that inactivity leads to fatness, and this is reflected in a series of public health initiatives aimed at making children active. One study in UK has shown that fatter children are less active and this might be due to physiological and psychological explanations<sup>9</sup>. This then has implications for how one addresses the obesity epidemic as there needs to be a multifactorial approach encompassing both physiological and psychological supports and with children it cannot be done in isolation but with the family unit.

Epidemiological studies have suggested that metabolic programming is one of the contributing factors to the aetiology of obesity as well as concurrent increase in related chronic illnesses<sup>6</sup>. One hypothesis for this is over nutrition is the delivery of nutrients in excess of the needs required for normal growth, development and metabolism<sup>6</sup>.

Given all this it is also important to note that medications can also have significant effect on a patient's weight by affecting some of the brain neurotransmitters and receptors sites and thus affect how the body responds to food when taking the medication. Those medications that block the histamine 1 receptors (H<sub>1</sub>) are known to cause weight gain but the exact mechanism is not fully elucidated. Other receptors involved include the serotonin receptor 5HT<sub>2C</sub> so when both 5HT<sub>2C</sub> and H<sub>1</sub> are blocked at the same time patients can experience weight gain<sup>7</sup>.

## Medications can affect weight

### Putting weight on

**Atypical antipsychotics** and conventional **antipsychotics** that have most potent antagonist actions on both H<sub>1</sub> and 5HT<sub>2C</sub> receptors have shown the greatest weight gain in adults<sup>7</sup>. Correll suggests that the gain might be even greater in children<sup>11</sup>. This weight gain and associated abnormalities in lipid and glucose metabolism and following association to diabetes, dyslipidemia, and hypertension and leading risk factor for future cardiovascular morbidity and mortality. Although there have not been significant long term studies of these medications in paediatrics let alone the disability population from the adult data, it can be assumed that there will be an increased risk of cardiometabolic syndrome and future cardiovascular morbidity and mortality<sup>11</sup>.

More and more are using antipsychotics and there is a known link in the adult populations between the use of antipsychotics especially amongst the schizophrenic population and increase in type II diabetes. This risk increases with the number of individual drugs prescribed but also differs considerably between medications<sup>8</sup>.

Associated weight gain from adult studies<sup>12</sup>

medication	Weight gain
chlorpromazine	+++
haloperidol	+
Amisulpride	+
Aripiprazole	+
asenapine	+
clozapine	+++
olanzapine	+++
paliperidone	+
Quetiapine	+
risperidone	+
ziprasidone	-

**Mood stabilisers** this includes sodium valproate, carbamazepine, and lithium have all been shown to cause weight increase but the mechanisms of action for this adverse effect has again not been elucidated. But it has been shown in Correll's meta-analysis that the combination of mood stabilisers and antipsychotics that the ad-

ditive effects of the combination are greater than when the individual medications are combined<sup>11</sup>.

Lithium is associated with weight gain and in adults is a significant contributor to poor medication adherence. This is because lithium can increase body's thirst and the increase in weight could be correlated with increase in high caloric drinks used to quench the thirst. Lithium also increases insulin secretion and thus increases adipose tissue leading to increased BMI (body mass index)<sup>12</sup>.

**Tricyclic antidepressants** such as amitriptyline, clomipramine, and imipramine, these all have effects on histamine receptors H<sub>1</sub> and thus have effects on weight gain. Carbohydrate craving has been reported with tricyclics and this contributes significantly to weight gain<sup>12</sup>.

### Weight neutral – can put weight on or off

When one is depressed, one of the symptoms can be increased or reduced appetite and it has been shown in clinical trial initially **selective serotonin reuptake inhibitors** (SSRIs) increased metabolic rate, suppressed appetite and increased basal body temperature. Over time though the initial weight loss wears off, there can be gradual weight gain thus making SSRIs weight neutral<sup>12</sup>.

### Can lose weight

**Psychostimulants** such as methylphenidate and dexamphetamine have been reported to cause weight loss; a clinical trial showed more marked weight loss in heavier children with methylphenidate. For a long time psychostimulants had the reputation of causing growth delay but this has been disproven in long term studies.

**Topiramate** is an antiepileptic has been shown to cause weight loss and at one time it was considered as adjuvant therapy for patients who have gained considerable weight but clinical trials have not been successful and serious adverse effects have also been noted,

There are other medications that have been used to cause weight loss and this includes fenfluramine and sibutramine, both of which have been removed from the Australian market. There are studies using the antidiabetic drug metformin in obese children who have developed type 2 diabetes with modest reduction in weight and blood glucose control but as with all medi-

cation there are adverse effects and these include an excess of lactic acid in the body which can cause pain and discomfort.

So when excessive weight gain is attributed to medication is noted then there tends to be a medication change to a more weight neutral medication. But changes in eating habits and exercise can also help in the effectiveness of any weight loss programme

**Summary of non medication approaches:**

- increase consumption of fruit and vegetables, as well as legumes, whole grains and nuts;
- limit energy intake from total fats and shift fat consumption away from saturated fats to unsaturated fats;
- limit the intake of sugars; and be physically active - accumulate at least 60 minutes of regular, moderate- to vigorous-intensity activity each day that is developmentally appropriate.

In recent study on Arizona showed that Autistic children have statistically significant differences in their metabolic and nutritional status when compared to non sibling match neurotypical controls<sup>4</sup>. This study showed that the autistic group had decreased biomarkers which include vitamins leading to increased oxidative stress, reduced capacity for energy transport and elimination of waste products. This can be expressed as variations in severity of autism. So healthy eating covering all the food groups is important but can be difficult with autistic children let alone with the added burden of medication increasing the carbohydrate craving. Switching options offered from high to low GI products can also help.

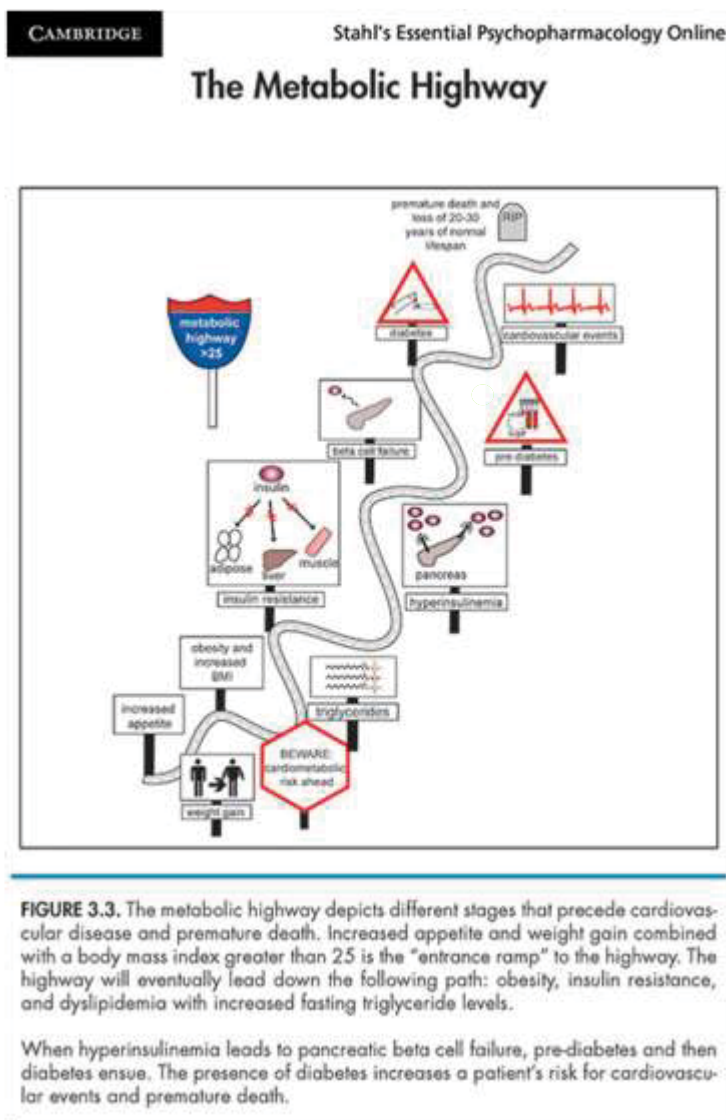
**Summary**

Obesity is increasingly prevalent in childhood and adolescence. Family doctors are well placed to manage this problem. Effective management of obesity in this age group will include:

- having a family-focused approach, especially with pre-adolescent patients
- setting small, achievable goals for behaviour change
- targeting sedentary behaviour
- helping families and young people to make healthier food choices
- providing ongoing support as families and young people make sustainable lifestyle changes<sup>3</sup>.

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**FIGURE 3.3.** The metabolic highway depicts different stages that precede cardiovascular disease and premature death. Increased appetite and weight gain combined with a body mass index greater than 25 is the "entrance ramp" to the highway. The highway will eventually lead down the following path: obesity, insulin resistance, and dyslipidemia with increased fasting triglyceride levels.

When hyperinsulinemia leads to pancreatic beta cell failure, pre-diabetes and then diabetes ensue. The presence of diabetes increases a patient's risk for cardiovascular events and premature death.

