

## Type 1 diabetes mellitus in children in Papua New Guinea

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### SUMMARY

Anecdotal and published information suggest a low incidence and prevalence of type 1 diabetes in Papua New Guinea (PNG). Incidence and prevalence were followed prospectively from July 1996, using the PNG Paediatric Surveillance Unit (PSU). No children were receiving insulin in Papua New Guinea at the start of the period. Over the next 4.5 years, 8 cases were reported – an annual incidence of 0.08/100,000 children aged <15 years and a prevalence of 0.28/100,000 aged <15 years. These figures are as low as any reported elsewhere. Three cases were from the small expatriate population. All cases in Melanesian children posed significant management problems, with two children dying during the study period.

### Introduction

The incidence of type 1 diabetes in childhood varies over 350-fold around the world (1). Anecdotal and published information suggest a low incidence and prevalence of childhood type 1 diabetes mellitus in Papua New Guinea (PNG). In July 1996 we commenced monitoring the incidence and prevalence through the PNG Paediatric Surveillance Unit (PNGPSU) and documenting the progress of cases. We also searched the literature for reports of the condition in PNG.

### Methods

1. The published literature on diabetes in Papua New Guinea was reviewed for mention of type 1 diabetes, or diabetes in children.
2. Senior paediatricians in the country were asked about their experience with type 1 diabetes in children.
3. Prospective surveillance.

Prospective surveillance was carried out using the Papua New Guinea Paediatric

Surveillance Unit. The PNGPSU was established in 1996, as an initiative of the Paediatric Society of PNG and HOPE *worldwide* (PNG). The PNGPSU is modelled on the Australian and British PSUs. It aims to document incidence, prevalence, clinical features and natural history of rare but important paediatric disorders, and to educate physicians and facilitate research about such conditions.

Monthly reporting cards are sent to every paediatrician in the country, and also some general physicians in isolated areas. The mailing list is about 34 to 40 each month. Cards are returned whether there are any positive reports or not. Case reports are followed-up by investigators. The definition used was 'Any child under 15 years with diabetes mellitus requiring daily (or more frequent) insulin injections'. Response rates to the return of reporting cards average around 76%.

Secondary ascertainment was attempted by contacting all hospital and private pharmacies in the country in 1998, asking them if they had seen any cases in the last year, and if they had any children on insulin.

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Full clinical details were obtained on each child, and the progress of each child was either directly or indirectly monitored.

## Results

### Literature and anecdotal reports

The diagnosis has been extremely rare in Melanesian children in the capital Port Moresby (serving a population now over 400,000): from the early 1960s until 1996, only one case could be remembered, along with a couple of reports mentioned in the literature in the 1970s (2,3).

Type 1 diabetes cases are very rare in the adult diabetes clinics as well. Only three cases are known to us (via personal observation, and personal communications from Ashim Sinha and Joe Kaven) – 2 in Rabaul and 1 in Port Moresby. The latter clinic has over 2000 patients registered. All 3 cases are now young adults, having developed diabetes in their late teenage years. This anecdotal information is supported by data showing a low frequency of anti-glutamic acid decarboxylase (GAD) antibodies in the Port Moresby Diabetic Clinic (4).

Fibrocalculous disease of the pancreas resulting in diabetes has also been reported in Papua New Guinea (5,6). The youngest case reported was 15 years old at diagnosis.

### Prospective surveillance – Paediatric Surveillance Unit

As at July 1996, there were no children under the age of 15 years receiving insulin for diabetes throughout PNG. 8 newly diagnosed cases were reported over the next 4 years and 6 months (until December 2000). 5 were in PNG-born Melanesian children and 3 in caucasian expatriate children (all born overseas, 2 in Australia and 1 in Finland). 2 of the 5 reports in PNG-born children were from the highlands, and 1 each from the other three regions of the country (Southern, Momase and Islands). 5 of the 8 children were girls. Age at diagnosis ranged from 4 to 12 years. The cases were reported evenly – 2 in the second half of 1996, 2 in 1997, none in 1998, 2 in 1999 and 2 in 2000.

The population aged under 15 years was approximately 2.15 million (preliminary results of the year 2000 census of the total population combined with age-bracket figures from the 1990 census): so the annual incidence was 0.08/100,000 population below 15 years of age and the prevalence (at December 2000, with 6 cases) 0.28/100,000 population below 15 years of age. These figures are remarkably low.

Secondary ascertainment is difficult in PNG. There is no independent registry. We contacted all hospital and private pharmacies in the country, with no new cases reported at all for 1998 (despite there being 3 on treatment at the time). However, the paediatric community is small and meets and communicates regularly. Discussions at various forums have led us to be almost certain that there are no other children in the country on insulin.

### Progress of the children

Management was often difficult due to limited health resources, poverty, isolation and lack of trained educators. Of the 5 national children, 2 have died – one following recurrent episodes of diabetic ketoacidosis, the other of unknown immediate causes. A third child, likely to be suffering from insulin-deficient type 2 diabetes, refused treatment and remains alive but unwell with visual problems, wasting and infections. The two other children are doing well, both benefiting from the new International Diabetes Federation (IDF) sponsorship program (7).

The three expatriate children are all doing well.

### Discussion

Type 1 diabetes varies in incidence from 36 per 100,000 children below 15 years of age/year in Finland and Sardinia to 0.1/100,000/year in China and Venezuela (1). The incidence of 0.08/100,000 we report here is thus as low as any reported. Generally, tropical countries have much lower incidences than temperate countries. The reasons for this are not clear. Certain HLA-DR-DQ genotypes increase risk (8), and these genotypes may not be uniformly distributed across populations. Some data suggest a protective effect of

breastfeeding and a harmful effect of early introduction of cow's milk, but the evidence is conflicting. In this context, Papua New Guinea has a relatively high rate of breastfeeding, and use of cow's milk is low due to its expense. Some enteric infections have been linked with the triggering of an autoimmune response (8). Once again, these viruses may vary in distribution across countries. There may also be other environmental factors operating, for example benefit from some aspect of the traditional diet.

It is possible, given the limited resources and isolation of many parts of the country, that some cases die before medical assessment, or are misdiagnosed (possibly as pneumonia or gastroenteritis). However, adult-onset type 2 diabetes is frequent in parts of PNG (2,9), and so health professionals are familiar with the clinical features.

Papua New Guinea has a relatively small non-Melanesian population – about 1% of the total population. However, 3 of the 8 cases reported were in expatriate children. These three children were all caucasian, born outside Papua New Guinea, and developed diabetes in PNG. Two were from the largest expatriate community in the country – Australia, a temperate country with a moderately high incidence of diabetes – and one from Finland – of which there is a very small expatriate community in PNG, but the home country has the highest incidence of any in the world (1). There is a long preclinical phase to the disease, and it is likely that these children acquired prediabetes before moving to PNG.

The death of 2 of the 5 national children is unfortunately not surprising given that comprehensive management of childhood diabetes is very difficult in PNG. There are only three trained (adult) diabetes educators in the country, all in the capital Port Moresby, and very few physicians have experience with children with the condition. Insulin is available in most provincial hospitals, and insulin and syringes are provided free or at a very small cost by the Government. However, blood glucose monitoring is not supported by the Government, and so families must purchase glucometers and testing strips at premium prices through private pharmacies. Aside from

the provincial hospitals, nearly all health facilities in the country cannot test blood glucose.

Beyond these difficulties with obtaining supplies, further obstacles face many families, including low literacy and education levels, lack of refrigeration for insulin and the isolation of many communities.

The IDF has commenced a program linking sponsors in developing countries with diabetes centres in developing countries, to ensure adequate supplies of insulin, the capacity to self-monitor and education (7). The three pilot countries are the Philippines, Fiji and Papua New Guinea. This program is already giving assistance in Papua New Guinea, and will be further needed as children with type 2 diabetes are diagnosed. Also, treatment guidelines suitable for PNG have been developed and are published as an appendix to this paper as well as in the child health manual for PNG doctors.

In conclusion, type 1 diabetes has an extremely low incidence and prevalence in Papua New Guinea, as low as any reported in the world. The reasons for this are not yet clear. The rarity of cases, difficult logistics and lack of resources make management of this condition challenging.

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#### APPENDIX

### Management of diabetes mellitus in children in PNG

To date, most reported cases have been type 1, or insulin-dependent diabetes mellitus. Usually the children are lean, with a short history of symptoms, and an absence of family history. It is more common in expatriate children.

Type 2 (non-insulin-dependent diabetes) may also be seen, particularly in overweight adolescents from coastal regions. Fibrocalculous disease of the pancreas (which results in diabetes and is associated with malnutrition) is also seen occasionally.

Diabetes is a complex disorder. In type 1, life-threatening crises (hypoglycaemia or ketoacidotic coma) are frequent unless well managed. In all types, complications (kidney, eye, nerves, heart) will develop without good control. Optimal management is by a multidisciplinary team (physician, diabetes nurse educator, dietitian, social worker) but good results may be obtained by careful management in the provinces.

#### Presentation

The commonest symptoms of diabetes are polyuria, polydipsia and weight loss. Also frequent are nocturia/enuresis, visual

disturbance, abdominal pain and vaginal itch or thrush. Symptoms will steadily progress. Type 1 diabetes patients without treatment will develop ketoacidosis. Ketoacidosis presents as decreased consciousness or coma, vomiting, dehydration, abdominal pain, Kussmaul-type hyperventilation and the smell of ketones.

Differential diagnosis includes urinary tract infection, diabetes insipidus, renal disease and stress hyperglycaemia. It is important to think of diabetes in atypical cases of severe abdominal pain, tachypnoea due to 'pneumonia' and 'gastroenteritis'.

#### Diagnosis

The diagnosis is made by demonstrating a persistently elevated blood sugar level (BSL). Glucose tolerance tests are almost never necessary in type 1 diabetes but are useful in type 2 cases. Therapy should commence immediately after diagnosis – don't send the child home to come back to clinic! An abdominal X-ray should be done to exclude fibrocalculous disease of the pancreas. Urea and electrolytes, and blood gases if unwell, should be measured, urinalysis should be performed, and sometimes a chest X-ray or examination of a mid-catch urine specimen is indicated.

#### Treatment of type 1

Two types of insulin are used: short-acting (Actrapid, Humulin R or similar) and long-acting (isophane – Humulin NPH or similar). NB – insulin is usually in the strength of 100 U/ml, so 10 U = only 0.1 ml.

#### Ketoacidosis

- If shock is present, resuscitation should be carried out with 10-20 ml/kg of normal saline or Haemaccel given quickly.
- Insulin must be commenced as soon as possible. Short-acting insulin 50 units is loaded into 50 ml of normal saline and given at 0.1 ml/kg/hour (equating to 0.1 U/kg/hour of insulin) in a side-drip. If an infusion cannot be loaded quickly, commence therapy with 0.1 U/kg given subcutaneously or intramuscularly, every hour.

- Fluid needs should be calculated from maintenance and deficit, and then administered initially as normal saline, half of the 24-hour requirement given in the first 8 hours and the remainder in the next 16 hours. Monitor BSL half- to one-hourly. Once the BSL has fallen to 12-15 mmol/l, fluids should be changed to 4% dextrose and 0.18% saline (or half normal saline made up to 5% dextrose if available). Do not stop the insulin infusion. It is often necessary to add extra dextrose to the saline/dextrose infusion to maintain BSL above 4 mmol/l. Electrolytes, pH and urine ketones should be monitored every 2-4 hours. Substantial potassium replacement is necessary, and should be commenced as 30 mmol/l of fluid as soon as urine output is confirmed.
- Intravenous bicarbonate is only very rarely indicated, and may be harmful in some cases.
- Cerebral oedema is a rare but catastrophic complication of management. Excessive fluid administration should be avoided, and hypernatraemia poses added dangers. If cerebral oedema is suspected, mannitol should be administered immediately.
- This is a life-threatening condition – advice should be obtained from experts if you are inexperienced.

*Once ketoacidosis has resolved, or initial therapy if not ketoacidotic*

- Commence regular insulin as below, starting at 0.25 U/kg/day in two divided doses.

Two-thirds of the daily dose should be given 30 minutes before breakfast and one-third 30 minutes before the evening meal. On each occasion, two-thirds is given as 'long' acting and one-third as 'short' acting. Titrate dose to response, aiming to avoid hypoglycaemia and keep BSL 4-8 mmol/l. Generally around a total of 0.5 U/kg/day is needed for prepubertal children, and 0.5-1.0 U/kg/day for pubertal children. Insulin requirements may fall temporarily in the first few months (the 'honeymoon period').

#### *Long-term management*

Details are beyond the scope of this article; protocol books and parent information manuals can be obtained on request from HOPE *worldwide* (PNG). Caloric intake should be spread through the day, with three meals and six snacks, and regular exercise. As much as possible, the choice of foods should conform to the normal family diet. Simple carbohydrate ('sugar') foods, drinks and sweets should be avoided. BSL should be monitored with glucometers at home if possible, otherwise test urine. Parents and child need education on injection technique, diet, exercise, recognition and management of hypoglycaemia, 'sick days' and recognition of ketosis. Much encouragement and support is needed. Complications should be monitored for, and managed appropriately.

#### **Treatment of type 2**

Management of type 2 in children is similar to that in adults. Specialist advice should be obtained.