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Public Health Spotlight

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Hon. Sabrina Turner, MP

Minister for Health & Wellness

This is a very important issue of the Public Health Spotlight, and I am grateful for the contribution which HSA's Genetics Coordinator, Joy Merren, has made to this month's edition via her piece on *Genetic Disorders in the Cayman Islands*.

February is recognised among certain countries in the world as Rare Disease Month, with the 28th of the month marking Rare Disease Awareness Day.

The aim of this observance is to raise awareness of rare diseases and improve access to treatment for these individuals.

Persons who have rare diseases or disorders, as well as their family members and other loved ones, will often note that treatment for many rare diseases is insufficient, as are the support networks.

Many of the genetic disorders highlighted in this month's issue are considered rare, and while this is not an exhaustive list of all rare disorders and/or diseases present on island, it is a starting point for that dialogue.

My team at the Ministry of Health and Wellness has been working to determine the prevalence of our nation's most prolific non-communicable diseases, such as heart disease and diabetes, because we know the impact that they are having on a large segment of our population.

However, we cannot solve the issues of access to and equity in health care if we focus solely on the needs of the majority.

After all, our remit is the health and wellness of the entire nation.

At your service.

Genetic Disorders in the Cayman Islands

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In 1950, the Saturday Evening Post published an article on "The Islands That Time Forgot", referring to the Cayman Islands. The description was appropriate not only in how it captured Cayman's isolation to the rest of the world, but also the internal isolation that happened between districts within our own shores.

Whenever there is such stark isolation, regardless of where it is in the world, there tends to be consanguinity. Consanguinity is defined as the fact of being descended from the same ancestor, meaning that a couple are blood relatives. For instance, there is an increased risk of cousins marrying cousins. With consanguinity, there is also the increased risk of autosomal recessive disorders. Cayman was no exception.

Autosomal recessive disorders:

Autosomal recessive is a pattern of inheritance characteristic of some genetic disorders. "Autosomal" means that the gene in question is located on one of the numbered, or non-sex, chromosomes. "Recessive" means that two copies of the mutated gene (one from each parent) are required to cause the disorder. In a family where both parents are carriers and do not have the disease, with each pregnancy, there is a 25% risk of the child having the disease, 25% of the child not having traits or disease, or 50% chance of the child having the trait (ie: being a carrier).

Cayman Ataxia

Persons with Cayman ataxia have delayed developmental milestones regarding motor, speech, and mental ability. There are prominent cerebellar dysfunction, including incoordination of voluntary muscles, intention tremor, dysarthric or stuttering speech and wide-based ataxic gait, pes planus, scoliosis, eye abnormalities including nystagmus (twitching of the eyeball) and esotropia (cross-eye) or exotropia (lazy-eye). This disorder is non-progressive so persons can live a normal lifespan. However, some level of supervision is required. A study was done, and in 2003 the ATCAY gene was identified.

Table 1: Age and Gender Profile of Patients with Cayman Ataxia

Age (years)	Male	Female
0-5	0	0
6-17	<5	<5
18-45	<5	0
46-59	<5	6
60 & >	5	5
%	<50%	>50%

Total: 22

Ataxia is a term for a group of disorders that affect co-ordination, balance and speech.

Sanfilippo Syndrome Type A

All four subtypes of Sanfilippo syndrome relate to central nervous system deterioration.

Individuals with this condition are missing, or have a dysfunctional version of, a key enzyme necessary to break down long chains of sugar molecules called mucopolysaccharides, or glycosaminoglycans (GAGs).

Without this enzyme, the molecules build up in the body. This accumulation can lead to severe brain damage and regression in development.

Sanfilippo Syndrome Type A is one of the four subtypes of Sanfilippo syndrome, a rare neurodegenerative disease that appears in early childhood. In Sanfilippo Syndrome Type A there is a deficiency in the enzyme heparan N-sulfatase that is needed to break down heparan sulfate. Because there is not enough of this enzyme, the heparan sulfate stores up in the central nervous system and in various organs in the body.

It is a progressive disorder. Babies appear normal at birth and there is normal development until the child reaches 2 or 3 years old. The stages are as follows:

Stage 1: start to lag regarding the developmental milestones; hyperactive

Stage 2: extremely restless; aggressive; language gradually lost; regression in toilet training

Stage 3: unsteady on feet; unable to walk; unable to care for self; severe neurologic degeneration occurs; total care needed.

Death usually occurs in mid-teens. There were eleven persons with this disorder, but presently there are no persons with it known to the Public Health Department. A study was done, and the gene mutation was found.

Usher Syndrome

Usher syndrome is an autosomal recessive disorder in which there is congenital deafness, and the person develops retinitis pigmentosa. There are three types of Usher syndrome found worldwide.

A study was done locally, and the gene mutation was found on chromosome 1 – Usher Type 2A. Clinical manifestations include decreased hearing from birth (non-progressive) and retinitis pigmentosa which begins in young adulthood (progressive).

Table 2: Age and Gender Profile of Patients with USH2A

Age (years)	Male	Female
0-5	0	0
6-17	0	0
18-45	0	<5
46-59	5	<5
60 & >	<5	<5
%	>50%	<50%

Total: 15

With retinitis pigmentosa, first the rods begin to degenerate leading to night blindness; then the cones degenerate leading to tunnel vision. Blindness usually begins in older adulthood.

There are also some persons with Usher Type 1 in Cayman. However, the largest kindred in Cayman are of persons with Usher Type 2A.

Apolipoprotein CII Deficiency

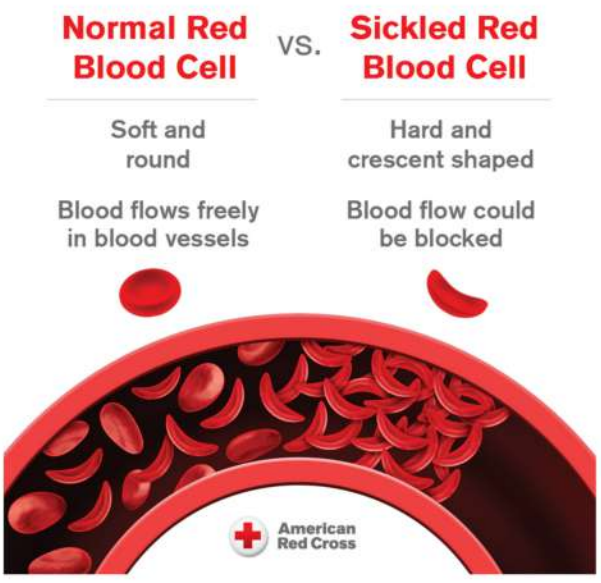
With Apolipoprotein CII deficiency, apo CII is deficient so the enzyme (lipoprotein lipase) is not activated, leading to high triglycerides. Acute pancreatitis can be a complication. The patients need to be on a very low-fat diet, and are placed on medication. Presently there are fewer than five adults living in Cayman with this disorder.

The Cayman Islands are now no longer "The Islands that Time Forgot" but they have been transformed into a multinational, multicultural society with a much larger gene pool. Because of this, the prevalence of these four disorders (Cayman ataxia, Sanfilippo Syndrome Type A, Usher Syndrome, and Apolipoprotein CII deficiency) has decreased as the gene pool has increased and become more diversified.

In 1997, the Cayman Islands Hospital began routinely performing cord blood haemoglobin electrophoresis on babies born at the Cayman Islands Hospital in Grand Cayman and at Faith Hospital in Cayman Brac. In 2002, the Cayman Islands Hospital expanded neonatal screening services by implementing Neo Gen Screening (now PerkinElmer Genetics) comprehensive newborn screening for over 50 inherited disorders. CTMH Doctors Hospital also offers PerkinElmer Genetics newborn screening.

Sickle Cell Disorder

Sickle cell disorder is included in the newborn screening. It is a group of inherited disorders that affects red blood cells. Normal red blood cells are round, flat and very flexible. However, when oxygen comes out of the sickled cell, the cell becomes stiff and takes on the shape of a sickle – hence, the name.



A normal red blood cell lives for approximately 120 days but a sickle cell may live only 11 or 12 days, resulting in haemolytic anaemia. The four most severe types of sickle disorder are Hb SS disorder, Hb S/beta0 thalassaemia disorder, Hb SC disorder and Hb S/beta+ thalassaemia disorder.

Table 3: Population Profile: Sickle Cell Disease

Type of Sickle Cell Disease	0-5 years	6-17 years	18-45 years	46-59 years	60 & > years
Hb. SS	<5	6	6	<5	0
Hb. SC	<5	<5	6	<5	<5
Hb. S/ beta0 thalassemia	0	0	0	<5	0
Hb.S/beta + thalassemia	0	<5	6	0	0
Age Groups-all 4 types	<5	11	18	9	<5
%	<10%	≈25%	>40%	≈20%	<10%

Total: 44

The disorders are clinically variable. These disorders can be severe. The mode of inheritance is autosomal recessive.

In the Cayman Islands, approximately 0 to 2 babies are born each year with sickle cell disease. The percentage of sickle positive births between 1997 and 2021 has varied from 1.9% to 8.4% each year. However, 5.4% of the total births had either sickle cell trait (patient remains healthy under normal circumstances) or sickle cell disease. The frequency of the sickle trait in the Cayman Islands is lower than the quoted values for the Caribbean in general (which is 10%).

Hemoglobin Bart's Trait

Normally, a person inherits four genes (two copies on each chromosome 16) that are responsible for globin chain production (two from each parent). Alpha thalassaemia is caused by a decrease in the amount of alpha globin chains produced.

- Silent Carrier (single gene deletion): only three out of the four genes are inherited
- Alpha Thalassemia Trait (two gene deletion): only two genes are inherited
- Hemoglobin H disease (three gene deletion): only one gene is inherited
- Foetal Hydrops Syndrome (four gene deletion): no genes are inherited

In the silent carrier, the person is clinically normal, and no special medical care is needed as the three genes compensate almost completely. A small amount (< 5%) of Hb. Barts is present at birth, but this later disappears.

With alpha thalassemia trait, the person may be mildly anaemic, but no special care is needed. A small amount (between 5 and 10%) of Hb. Barts is present at birth, but this later disappears.

With Hemoglobin H disease, the person has only one alpha globin gene. This patient can have mild to moderate anaemia, sometimes with enlarged spleen or with gallstones. He/she may need occasional blood transfusions, and there is an increased risk for infections. With Hb

H disease, there would be a large amount of Hb Barts at birth and it will probably not disappear from the blood (unlike Barts trait). Hb H disease is rare in persons of African descent, where the *trans* form is much more common than the *cis* form.

With Hydrops foetalis, there are no genes to produce alpha globin. Infants with this do not survive, as they are unable to make enough Hb. Stillbirth is frequent, or some newborns may live only a few hours.

In Cayman, approximately 3 to 19 babies are born each year with Hb Barts trait. The percentage of Hb Barts trait births per year (excludes 2003 to 2005 when Hb Barts screening was not done by NeoGen Screening) has varied from 0.4% to 2.5%. There have been no patients with Hb H disease based on the PerkinElmer Genetics newborn screening results.

G6PD deficiency

G6PD is the abbreviation for glucose-6-phosphate dehydrogenase – an enzyme found in the red blood cells that protects them, keeping the cells strong. If the child is exposed to a medication or infection that causes oxidative stress, the red blood cells are destroyed faster than the body can replace them, leading to haemolytic anaemia.

If there are signs/symptoms, the parent is advised to take the patient immediately to the patient's doctor or to Accident &Emergency. The child usually gets well on his/her own.

Occasionally, the reaction can be very severe, and the child may need a blood transfusion. Severity of the disease varies from child to child. The child with G6PD deficiency should avoid certain medications and substances.

Table 4: Age Profile of Patients with G6PD Deficiency

Age (years)	Patients (male and female)
0-5	122
6-17	309
18-45	35
46-59	0
60 & >	0

Total: 466

G6PD deficiency is passed down from parent to child by X-linked recessive mode. Approximately 7 to 38 babies are born each year with G6PD deficiency. The percentage of G6PD positive births between 2002 and 2021 has varied from 1.2% to 4.7%.

However, 3.4% of the total births from 2002-2021 had G6PD deficiency. The main type of G6PD deficiency that babies born in Cayman tends to be mild.

Gongenital Cataract

Congenital cataract is a type of cataract that presents at birth or during early childhood.

There can be various modes of inheritance but for this kindred, the mode of inheritance is autosomal dominant.

Table 5: Age and Gender Profile of Patients with Congenital Cataracts

Age (years)	Male	Female
0-5	0	0
6-17	0	0
18-45	<5	7
46-59	<5	<5
60 & >	<5	<5
%	<50%	>50%

Total: 16

A congenital cataract is when the lens of the eye is cloudy instead of clear at birth, making it hard to see. The lens is the tissue inside your eye that helps focus the light coming into your eye. Congenital cataracts can happen in one or both eyes. If congenital cataracts aren't treated early, they can cause vision problems or blindness.

Down Syndrome

Table 6: Age and Gender Profile of Patients with Down syndrome

Age (years)	Male	Female
0-5	<5	<5
6-17	10	6
18-45	8	6
46-59	0	<5
60 & >	0	0
%	>50%	<50%

Total: 33

Down syndrome is the most common chromosomal abnormality. There are three types but the most common (95% of the time) is Trisomy-21 where there is an extra chromosome 21 in each cell in the body.

However, this type is not inherited but instead caused by an error in cell division during early development of the foetus. Severity varies among individuals.

There are also other genetic disorders known to Public Health Department in which there are fewer than five persons with each disorder.

For more information on genetics clinics, counselling, testing, education, and support groups please email joy.merren@hsa.ky

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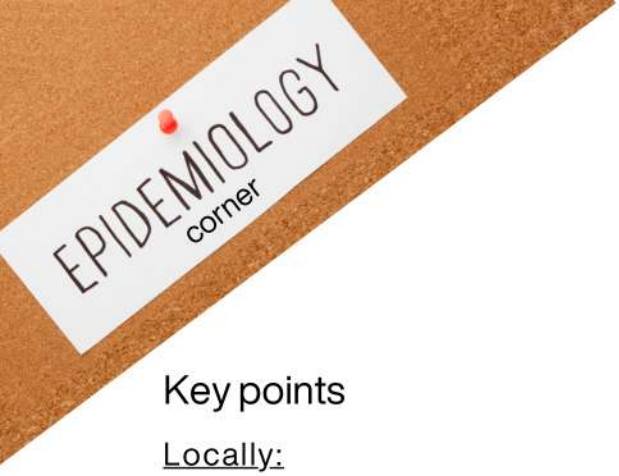

COVID-19 Surveillance Data

January 2023 (data as of 3 February 2023)

Key points

Locally:

In the Cayman Islands there were 17 COVID-19 hospital admissions in January 2023, which remains similar to the previous month of 16 COVID-19 hospital admissions. This includes individuals admitted for morbidity relating to their SARS-CoV-2 infection and those who test positive for COVID-19 when screened on admission and receiving hospital care for other medical needs. Two COVID-19 patients were admitted to critical care during January 2023. There were no COVID-19 deaths reported in January, and two COVID-19 deaths were reported in the previous month.**

An additional 432 Autumn 2022/2023 boosters were administered during January.

Genomic sequencing results from 83 positive SARS-CoV-2 samples in early December continue to present Omicron as the only variant currently circulating in the Cayman Islands. Among identified sub-variants, BA.5 and its descendant lineages are the most commonly detected (86%). The BQ.1 lineage attributed to 37% and BQ.1.1 attributed 20% of the sequenced samples. These trends align to the global picture, with BA.5 and its descendent lineages reported as dominant globally by WHO[1], and BQ.1 lineage is the predominant sub-lineage currently circulating in the UK[2]. XBB and XBB.1 variants were identified in the samples from early December 2022, however are not indicated to be a commonly detected sub-variants.

[1] World Health Organization, 2023. Weekly epidemiological update on COVID-19 – 8 February 2023. Available online: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---8-february-2023

[2] UK Health Security Agency, 2023. SARS-COV-2 variants of concern and variants under investigation in England: technical briefing 49. Available online: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1129169/variant-technical-briefing-49-11-january-2023.pdf

*** Effective immediately, the Ministry of Health & Wellness will report information relating to COVID 19 deaths on a monthly basis, via the Public Health Spotlight publication.*

Figure 1: Weekly hospitalisations and deaths (since 8 September 2021[d])

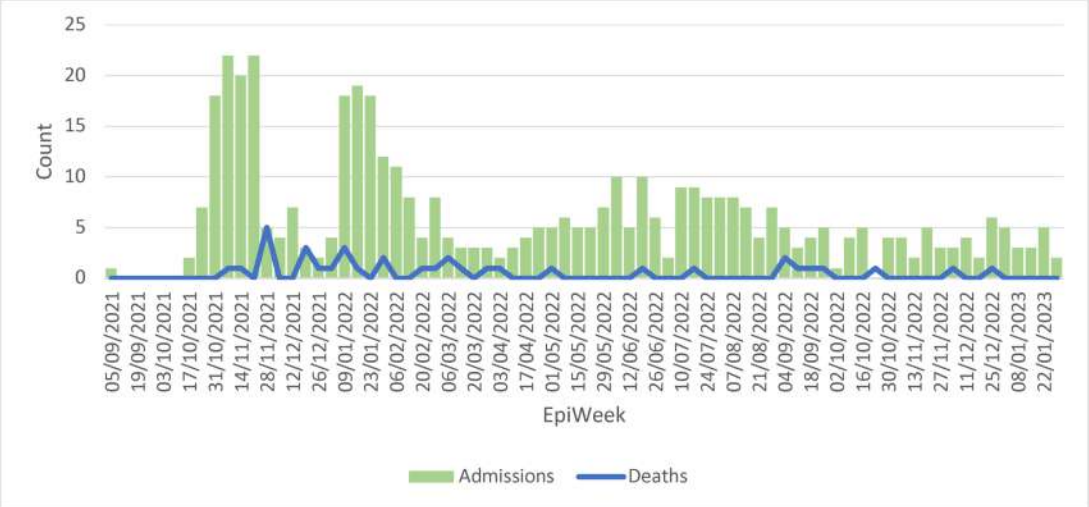

Table 1: COVID-19 patients admitted to hospital

Indicator	January 2023	December 2022	Percentage change
New COVID-19 patients admitted [a]	17	16	6%
New admissions with ≥ 2 doses of a COVID-19 vaccine	14	9	36%
COVID-19 patients discharged	14	15	-7%
Number of inpatients	21	21	0%
Supplemental O2 inpatients [b]	6	2	67%
ICU inpatients [b]	2	0	NA
Ventilated inpatients [b]	0	0	0%

[a] Admissions include patients who are detected as being COVID-positive on screening.

[b] Inpatient indicators are based on data received at the point of admission.

Table 2: COVID-19 vaccine uptake and coverage within the previous month.

Dose Number	Number administered January 2023	Total Count	Coverage of Total Population [c]	Coverage of population over 5 [c]
Primary course 1	73	61,932	86.7%	95.7%
Primary course 2	70	60,659	84.9%	93.7%
2021/22 Booster	0	24,064	33.7%	37.2%
2022 Booster	0	2,772	3.9%	4.3%
Autumn 2022/2023 Booster	432	1,955	2.7%	3.0%

[c] Based on a Total Population of 71,432.

Figure 2: Vaccine uptake over time

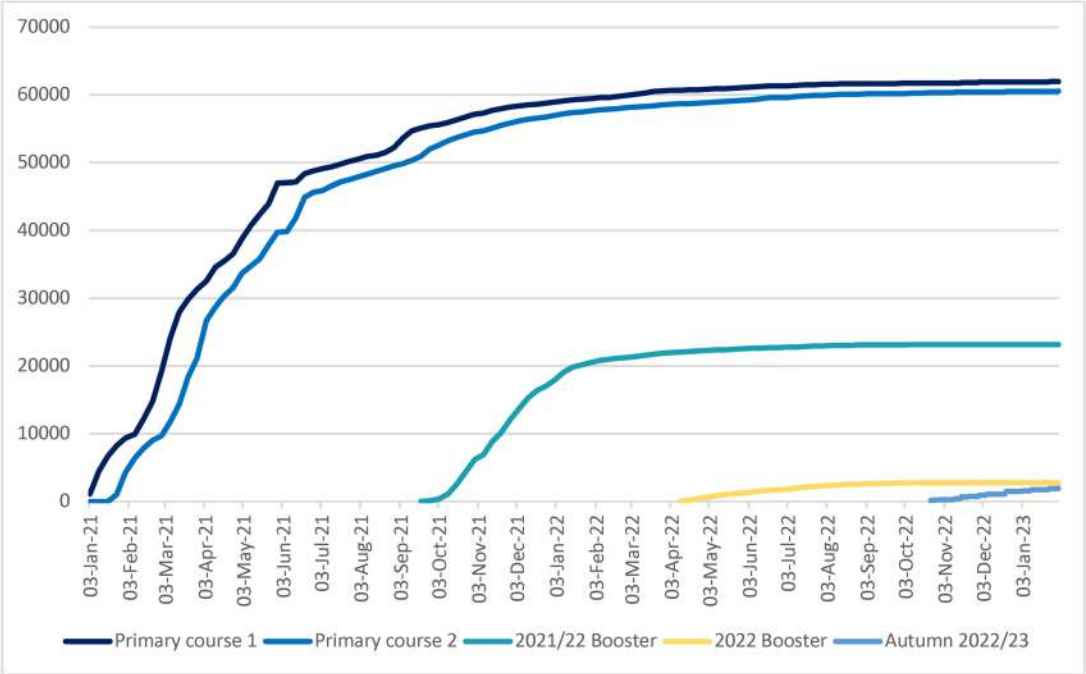

Figure 3: Cumulative Autumn booster uptake over time by age group.