In 1934, two severely mentally retarded children were brought by their mother to see Dr Asbjørn Følling, a Norwegian physician, having consulted numerous doctors to no avail. She had noticed that both children had a strange bodily odour.[1] Dr Følling eventually proved that these children, along with eight other severely mentally retarded children excreted phenylpyruvic acid in their urine leading to the description of oligophrenia phenylpyrouvica, later termed phenylketonuria.[2]

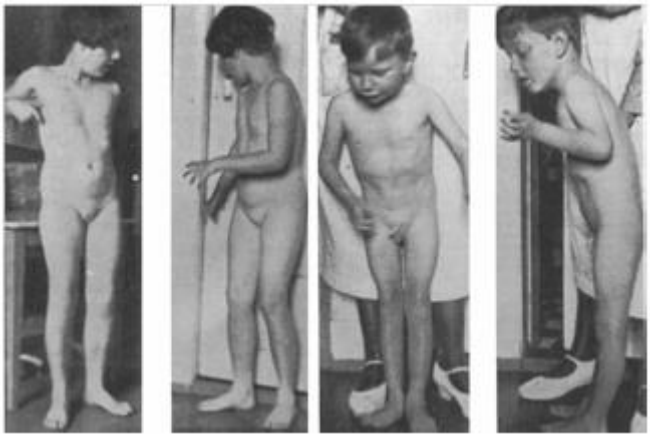

Figure 1:The two mentally retarded sibling whom their mother brought to see Dr Følling[2]

HOPPE-SEYLER'S ZEITSCHRIFT

für

PHYSIOLOGISCHE CHEMIE

Über Ausscheidung von Phenylbrenztraubensäure in den Harn als Stoffwechselanomalie in Verbindung mit Imbezillität

Sonderabdruck aus Band 227, Heft 1, 2, 3 u. 4

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Fig. 3. This publication from 1934 describes the discovery of phenylketonuria.

Figure 2:The publication from 1934 describing the discovery of phenylketonuria [2]and the scientist behind the discovery, Dr Følling[1]

Phenylketonuria (PKU) is an autosomal recessive disorder, characterised by an inborn error of metabolism caused by a deficiency of phenylalanine hydroxylase (PAH).[3] PAH is the hepatic enzyme necessary for the metabolism of phenylalanine (Phe) to the amino acid tyrosine using tetrahydrobiopterin (BH4) as a cofactor. The deficiency of PAH leads to the accumulation of Phe and its metabolites giving rise to the 'mousy' odour of the body and urine.[4] The pathophysiological mechanisms by which PKU causes neurological dysfunction are multiple and not well understood. It has been postulated that Phe may inhibit cortical neuronal growth and induce neuronal death and downregulate brain-derived neurotrophic factor (BDNF) which is critical for neuronal development and protection. [5] Hyperphenylalaninaemia also inhibits the hydroxylases of tyrosine and tryptophan leading to a deficiency in cathecholamines and serotonin.[6] If left untreated, is associated with microcephaly, epilepsy, severe mental retardation and, in some cases, progressive supranuclear motor disturbances. Other characteristics include gait abnormalities, behavioural problems such as hyperactivity, agitation or attention deficit and light skin pigmentation. These symptoms can largely be prevented by the early start of a phenylalanine-restricted diet, [7] hence the importance of early identification via the national newborn screening programs.

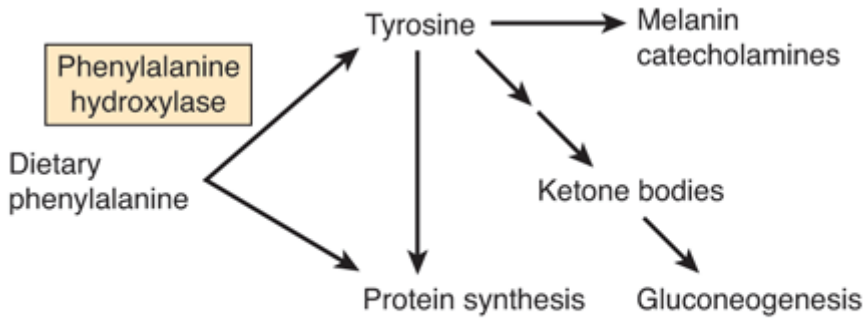

Figure 3. Metabolic pathway of phenylalanine. The deficiency of phenylalanine hydroxylase in PKU leads to the accumulation of phenylalanine and deficiency of tyrosine [8]

High phenylalanine concentrations are associated with ocular abnormalities and subclinical visual impairment as illustrated by a study of pattern reversal visual evoked potentials in patients with PKU.[9] Reported ocular abnormalities include photophobia, corneal opacities and cataracts.[10] Iris and fundus pigmentation of phenylketonurics has also been reported to be significantly lighter. [11] This

observed dilution is attributed to tyrosine being the immediate precursor to melanin, with the deficiency of tyrosine resulting in the interruption of melanin synthesis.

Even prior to modern photography, medical illustration has long been used to depict the eye. The ancient Greeks made anatomical drawings even as far back as 400BC. A realistic illustration of the retinal was drawn by Van Trigt in 1854. This was not long followed by the first published human retinal photography by Jackman and Webster in 1886.[12] The quality of early fundus images was however poor and the availability of early fundus photography was very limited.

Between the years 1940 to 1960, at the Royal Victorian Eye and Ear Hospital, Ilene Hill a medial artist painted the fundi of two patients at the Kew Asylum – Jack Pearce aged 23 and Gail T aged 9, both described to have Følling's disease. Jack had macular hypoplasia and Gail had a hypopigmented albinotic fundus (Fig 4).

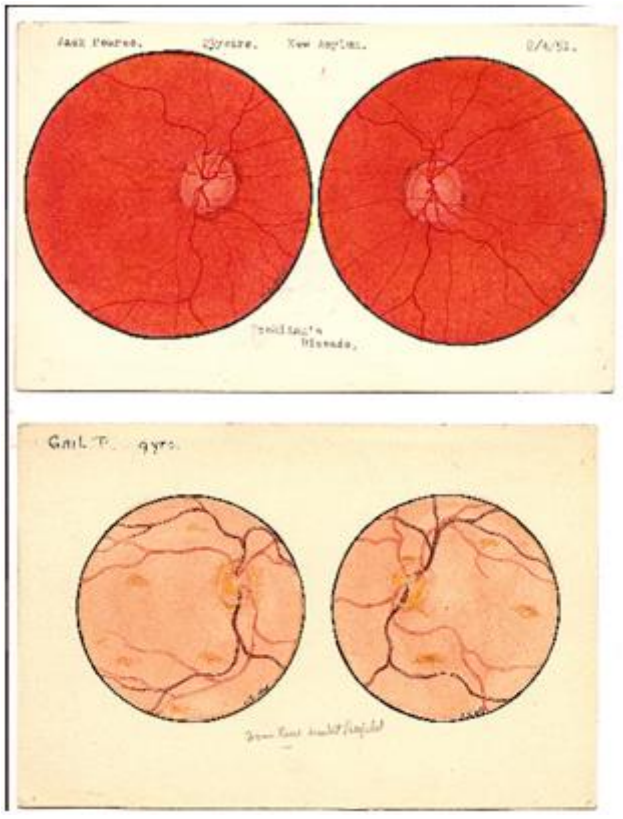

Figure 4: Painted fundi of the two phenylketonuria patients seen at Kew Asylum

The Kew Lunatic Asylum (Fig 4), later known as Willsmere was the largest psychiatric hospital built in Victoria and one of the grandest buildings constructed in Melbourne during the 19th century.[13] It was first opened in 1871 as a ward of Yarra Bend and was operational from 1871 to 1988. Designed to be a 'magnificent asylum for the insane', the institution was as notorious as it was renowned, for its internal horrors

and chequered history including overcrowding, mismanagement, poor sanitation and disease. In the early days, many wards of the state, 'difficult' children and children with mental retardation were housed with the adults at Kew. As the number of child inmates grew, the "Idiot Ward" was opened on the asylum's grounds in 1887. Later known as the Children's Cottages of Kew, these were established to provide accommodation and educational instruction for mentally retarded children.

Figure 5: The Kew Asylum, Kew, Victoria [15]

The discovery of phenylketonuria was a fundamental medical advancement made possible by a man such as Dr Følling, with his perseverence and insight in the face of then relatively little information and even less technology. History continues to be rewritten with emerging knowledge and technologies, allowing one of the causes of mental retardation to be reversible. The same can be said with the advancement of ophthalmic illustration, from the days of graphic illustration until now the era of modern photography.

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