Sometimes parents, physicians and the general public forget or take for granted how far paediatric medicine has come, particularly in areas such as childhood immunization and infectious diseases. Canadians need to remember the legacy of the gifts of health and longevity given to us by previous generations of physicians and scientists. This column recognizes these accomplishments and, hopefully, reminds us of our good fortune. As physicians who care for Canadian children, we are very grateful for the many medical achievements of the past. That is why the editorial board members of *Paediatrics & Child Health* feature the column, "Lessons Learned", to recognize these accomplishments.

Cretinism: The past, present and future of diagnosis and cure

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A cretin, from the French chrétien (Christian), is defined in Webster's Encyclopedic Unabridged Dictionary (1) as "one who is human despite deformities". The medical definition of cretinism is untreated congenital hypothyroidism, with or without a goiter. Iodine deficiency is still a major cause of endemic cretinism, but in Canada this is no longer true. An interesting historical reference to goiter in 1832 in the Ontario Native population stated (2):

> They are also very commonly subject to swelling of the neck usually called goiters...I have only to remark that the neck swells to a prodigious size without producing any pain, or other unpleasant effect.

The discovery of iodine and its importance in thyroid gland development and function toward the end of the 19th century eventually led to public health measures, which brought iodized salt to Canada shortly after the first world war. Iodine supplementation is a significant modern public health benefit. A quote from *The Boston Medical and Surgical Journal*, January 24, 1918 (3), on the dire (albeit erroneous) consequences of goiter in Alberta illustrates the major advances in scientific thinking since that time.

> Goitre is a disease which, when once acquired and not cured, can be transmitted even to the third and fourth generation of posterity, therefore people with this disease should not be permitted to indulge in parenthood.

Understanding the pathogenesis of congenital hypothyroidism has led to prevention, treatment and proper counselling.

Congenital hypothyroidism due to other causes occurs in one of 3500 live births. Before the introduction of neonatal screening, the diagnosis was often delayed until the second or third month of life, although greater delays in recognition were not unusual. Brain development is absolutely dependent on normal thyroid hormone levels. The fetus and the infant are neurologically vulnerable due to the incomplete brain development in humans at birth. A progressive intellectual deterioration occurs with each passing week in the absence of appropriate thyroxine replacement. Severe developmental and physical delays occur by six months of age. Treatment in infancy will reverse the physical changes, but not the neurological damage. Dr Jean Dussault (4), in the 1970s, then a young investigator from Quebec, saw some colleagues using filter paper spots to screen for phenylketonuria and tyrosinemia. He decided to see if thyroxine could be assayed from the same neonatal filter paper heel prick blood collection spots. He was enormously successful, and published the first report of preliminary mass screening in 1973 (5). He is credited with initiating what is now accepted as standard practice at birth

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as a means of the prevention of mental retardation secondary to congenital hypothyroidism (4). If congenital hypothyroidism is recognized at birth and treated immediately there is a very favourable therapeutic outcome. Many screening programs now use thyroid stimulating hormone eluted from the filter paper blood spots, but the principle is the same. Fortunately, in the clinic, we can no longer demonstrate to students the classic clinical signs of cretinism that were known to every paediatrician in the years before the onset of thyroid screening.

In the developed world, about 15% of people with congenital hypothyroidism have defects in thyroid hormone synthesis, and these individuals will often have a goiter. A small percentage of cases can be attributed to the transplacental passage of maternal blocking antibodies from mothers with autoimmune thyroiditis. However, the majority of cases are due to thyroid dysgenesis with ectopic/hypoplastic, hypoplastic or absent (agenesis) glands. The explosion of research in genetics and molecular endocrinology has given us some understanding of the factors controlling morphogenesis and migration of the thyroid in fetal life to the normal position in the anterior neck. A few defects are now known to be due to errors in fetal transcription factors controlling descent and configuration of the thyroid. Future research will complete our understanding of the development of the gland and thyroid hormone production (6,7).

The current recommendations for the initiation of treatment are thyroxine 10 to 15 µg/kg/day, crushed on a spoon and mixed in milk or water, but not put in the bottle so as to ensure full dose delivery. The tablets are sweet, and the taste is not unpleasant. In the past, the onset of treatment was often delayed longer than the current standard of 11 to 15 days, and the dose of thyroxine was lower (8). Normal short term developmental outcomes in even severely affected infants have recently been reported, with the early initiation of thyroxine at a dose of 9.5 µg/kg/day or higher and with maintenance of free tetraiodothyronine concentrations in the upper normal range during the first year (9). However, modifications in treatment recommendations may still be needed after further long term outcome analyses of screening and treatment schedules (8). Modern early discharge practices present a challenge, because the physiological surge of thyroid stimulating hormone in the first 24 h can cause false positive results, necessitating a recall of the infant for testing if the blood spot is taken too early. There are logistical difficulties with screening infants after discharge or following home birth, and these special situations need a careful solution.

The neonatal diagnosis and treatment of congenital hypothyroidism prevents severe intellectual delay, a significant contribution by many in the past century. The present century must address the needs of the millions of infants in nonaffluent parts of the world where congenital hypothyroidism of all etiologies, including iodine deficiency, is still a major health problem.

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