

A description of the aetiology of type 1 diabetes mellituse based on injuries to pancreatic nerves in infancy as a result of early weaning and subsequent bowel problems. Persistent straining injures these nervs resulting in loss of islets of Langerhans and loss of insulin production.

A detailed account is published in Medical Hypotheses, 2009 under “Diabetes, diet and denervation”, and, the idea recorded in American Journal of Medicine, 2008 and “Autonomic denervation and Autommune disease”. See [www.pubmed.com](http://www.pubmed.com)

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## Diabetes, diet and autonomic denervation.

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## **Abstract**

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Contemporary theories to explain the autoimmune aetiology of type 1 diabetes mellitus (T1DM) include the “hygiene”, “accelerator” and “thrifty phenotype” hypotheses though none accounts for its natural history, or, epidemiology. Early-onset, T1DM is much more common in Western countries and shares features of its epidemiology with other major childhood diseases.

In the autonomic denervation view, early-onset, T1DM results from injury to autonomic nerves supplying the pancreas through persistent physical efforts during defaecation in infancy. Pancreatic denervation results in loss of islets of Langerhans and reduced insulin production that may present in infancy or later life. Early introduction of cows milk and solids to the infants’ diet cause increased rates of bowel problems whereas exclusive breastfeeding in non-Western countries, protects the infant from both constipation and diarrhoea. Other important Western diseases may result from the varying effects of injuries to nerves at different sites in the autonomic nervous system.

**Key words; Type 1 diabetes mellitus, denervation, constipation, Western diseases.**

The incidence of early onset, T1DM is increasing rapidly in many Western countries (1). It doubled in Finland in the years 1975-2000 and will double again before 2020 (2). Studies of Finnish children show clear associations between early weaning (before three months of age) and the later onset of T1DM (3). These observations reflect previous, large-scale studies of breastfeeding, showing a protective effect against T1DM (4). Among many other valuable effects, exclusive and prolonged breastfeeding protects infants from bowel problems including constipation (5).

In the autonomic denervation hypothesis, persistent physical efforts during defaecation in infants result in injuries to autonomic nerves between the coeliac plexus and the pancreas (Fig 1). Pancreatic denervation leads to loss of islets of Langerhans, and, reduced levels of insulin. Adults suffering from defaecatory problems, injure their pelvic autonomic nerves in specific neuroanatomical patterns creating different patterns of pelvic pain (6). Reasons for the change in site of neuro-anatomical injury between adults and infants include (a) the change in body proportions, (b) the infant is often lying on it's back whilst undertaking physical efforts during defaecation, (c) the nerve supply to the pancreas is through short autonomic nerves as opposed to long hypogastric nerves supplying the pelvic viscera, and, (d) different patterns of physical efforts between children and adults.

Recent studies in T1DM show that early, selective loss of sympathetic nerves in the islets of Langerhans occurs in spontaneously diabetic rats (7). Preliminary studies show similar loss of nerves in human pancreas (8). Further evidence that sensory neurons

control insulin resistance and islet inflammation in diabetes-prone mice suggests an important role for pancreatic nerves in the pathophysiology of type 1 diabetes (9). Injury to autonomic nerves also results in release of nerve growth factor (NGF) whose molecular size and shape are similar to insulin and may contribute to diabetic neuropathy (10). Antibodies to insulin or NGF may have effects on the course of the clinical disease. Studies of fresh cadaveric material show the shape, extent and complexity of autonomic nerve plexi described by nineteenth century anatomists with which many contemporary clinicians are less familiar (Fig 1) (11). Many Western diseases show injuries to autonomic nerves including T1DM, cardiac arrhythmias, appendicitis, Crohns disease, ulcerative colitis, endometriosis, adenomyosis, fibroids, irritative bladder and irritable bowel, among many others (12).

Definitions of infant and childhood constipation vary though it affects 0.7-29.6% (median 9 %) of children; with half developing the condition in the first year of life (13). Peak prevalences occur at two to five years, affect both sexes equally, and constipation persists for many months or years. Changes in diet, including changing from breast to cows' milk, toilet-training, and, starting school, are common reasons for childhood constipation. Few studies distinguish between constipation and "straining during defaecation" though overall rates of constipation continue to increase in the age range of 0-2 years (14). Up to 40% of preterm babies (<28 weeks gestation) suffer constipation to the age of 14 years (15). Increasing rates of preterm delivery may contribute to some small part of the increasing incidence of T1DM though this effect may be small

compared to the decreasing rates of breastfeeding in many developed and Westernising countries.

Since the 1970's T1DM has been classified as an "autoimmune" disease. Autoimmune conditions typically occur in midline organs in later life, and, mainly in women, who also suffer an increasing incidence of progressive constipation associated with the late consequences of childbirth and hysterectomy (16). By contrast T1DM has a peak incidence in early life with equal sex distribution. Classical criteria for an "autoimmune" condition rely on showing circulating autoantibodies, recognising specific antigens for these antibodies, and, raising antibodies in experimental animals to produce characteristic pathological changes (17). No such antigen occurs in T1DM. Evidence suggesting an autoimmune aetiology includes detection of different autoantibodies, the histological appearances of the pancreas, and, associations with major histocompatibility antigens. Autoantibodies are non-specific, occurring in type 2 diabetes mellitus (5.3%) and normal controls (1.7%) (18). The histopathology of type 1 diabetes shows loss of beta cells in the islets of Langerhans and infiltration of the islets of Langerhans ("insulitis") by CD4 and CD8 lymphocytes (19). Accumulating macrophages result in less-specific histological appearances in the later stages of the disease. Persistent associations with major histocompatibility antigens in a minority of sufferers, have set the immunogenetic view firmly in place (20).

In adults, injuries to pelvic autonomic nerves result from persistent maternal voluntary efforts in the second stage of labour, straining during defaecation, and, some forms of

pelvic surgery (21-22). Injuries in labour result in collateral sprouting of nerve bundles and chaotic, nerve fibre proliferation throughout the stroma. Persistent, physical efforts in nulliparous women result in specific immunohistochemical lesions across the pelvis, and clinical presentations with pelvic pain (5). Injuries to endometrium and myometrium result in tissue hyperplasia resulting in adenomyosis (23) and leiomyomas (24) respectively. The disease phenotype in the adult pelvis depends on the site of injury to the autonomic nerves supplying the organ; the injury is to the “wiring” rather than the end-organ. In the autonomic denervation view of T1DM there is a postganglionic injury to short autonomic nerves between the coeliac plexus and the pancreas that results in loss of islets of Langerhans and insulin production.

Autonomic denervation may play a role in other important early childhood illnesses with similar epidemiological patterns (25-26). Acute lymphoblastic leukaemia (ALL) and asthma may result from splenic and pulmonary denervation respectively. Previous stochastic studies of the age of onset against the incidence, suggest a common origin for these three, major diseases of Western childhood (27). There are no recorded studies of splenic denervation in ALL though denervation in other generative organs such as the uterus results in tissue hyperplasia in the form of adenomyosis and leiomyomas respectively. Asthma, and other forms of atopy, are less frequent in breastfed infants, and, associated with airway irritability and bronchial reinnervation in many studies (28-29).

## Conclusions

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In the autonomic denervation view, persistent physical efforts during defaecation injure short nerves between the celiac plexus and the pancreas resulting in loss of islets of Langerhans and reduced insulin production. Prolonged breastfeeding prevents bowel problems in young children and may prevent the onset of T1DM in non-Western countries where exclusive breastfeeding for six months or longer, is the staple diet. The autonomic denervation view will be difficult to prove owing to difficulties in studying childhood bowel problems and the lack of availability of pancreas in the early stages of the disease owing to improved survival rates. Circumstantial evidence may be sufficient to persuade mothers to return to prolonged and exclusive breastfeeding to prevent this, and other, Western diseases.

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## Legend

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**Figure 1**

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Dissection of the coeliac plexus from a fresh cadaver with reflection of the head of the pancreas to demonstrate its nerve supply. Post-war preservation of cadaveric material in formalin destroys autonomic nerves obscuring much of the fine anatomical detail, originally described by nineteenth century anatomists.

(Courtesy of Professor XM Chang, Dept Radiology, North Sichuan Medical College, Sichuan, China.)