

Review of Vaccine Induced Immune Overload and the Resulting Epidemics of Type 1 Diabetes and Metabolic Syndrome, Emphasis on Explaining the Recent Accelerations in the Risk of Prediabetes and other Immune Mediated Diseases

J Barthelow Classen MD*

3637 Rockdale Road, Manchester, MD 21102, USA

*Corresponding author: J Barthelow Classen, 3637 Rockdale Road, Manchester, MD 21102, USA, Tel: 410-377-8526; E-mail: classen@vaccines.net

Received date: December 17, 2013; Accepted date: February 17, 2014; Published date: February 19, 2014

Copyright: ©2014 Classen JB. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

There has been an epidemic of inflammatory diseases that has paralleled the epidemic on iatrogenic immune stimulation with vaccines. Extensive evidence links vaccine induced immune over load with the epidemic of type 1 diabetes. More recent data indicates that obesity, type 2 diabetes and other components of metabolic syndrome are highly associated with immunization and may be manifestations of the negative feedback loop of the immune system reacting to the immune overload. The epidemic of diabetes/prediabetes appears to be accelerating at a time when the prevalence of obesity has stabilized, indicating that the negative feedback system of the immune system has been overwhelmed. The theory of vaccine induced immune overload can explain the key observations that have confounded many competing hypothesis. The current paper reviews the evidence that vaccine induced immune overload explains the disconnect between the increase in prediabetes and nonalcoholic fatty liver at a time when the obesity epidemic is waning in children.

Introduction

Twenty years ago it was predicted that a massive increase in immunization would result in a massive increase in people with chronic immune related diseases like type 1 diabetes, autoimmune diseases, and asthma [1]. A massive increase in immunization has occurred. In the United States for example since just 1999 children are scheduled to routinely receive over 80 additional vaccines over their childhood as explained below. The increase in immunization has been followed by a huge increase in inflammation associated disorders. Diseases like autism, type 1 diabetes, asthma, food allergies, many autoimmune diseases, obesity, type 2 diabetes, NASH and metabolic syndrome have increased many fold in children. The rate of change of several closely followed diseases appear to be accelerating while others have decelerated. This paper describes how the theory of vaccine induced immune overload can explain many observations about the changes in the epidemics.

Many hypothesis have been proposed to find alternate explanations for these epidemics, such as the hygiene hypothesis for autoimmune diseases and poor diet or decreased exercise for the obesity epidemic. These hypothesis don't readily explain the recent changes in the rates of these diseases. For example the prevalence of obesity in US children has stabilized while junk food and leisure activities persists, and the epidemics of autoimmune diseases continue to rise at a time where hygiene does not seem to increase.

Recently publications have provided evidence that vaccines are responsible for the epidemics of both autoimmune diseases such as type 1 diabetes as well as the epidemic of type 2 diabetes, obesity and metabolic syndrome [2]. One major problem with vaccines is the concept of one size fits all. Package inserts of almost all vaccines recommend a dose based on age. In order for a vaccine to be a commercial success it is expected to induce a protective immune response in well over 90% of children. In order for this to happen a

dose, based on age, must stimulate a protective immune response in those with the weakest immune system. In the process of doing this, the other 90% or more of children have their immune system over stimulated. The process of over stimulating the immune system time and time again increases the risk of inflammatory diseases like autoimmune diseases, and allergies which cause even more inflammation. The clinical manifestation of disease depends on one's physiologic response to inflammation as has previously been reviewed [3]. Inflammation causes the release of cytokines which can trigger autoimmune diseases but also stimulate cortisol production, the major negative feedback loop of the immune system. According to the theory inflammation induced cortisol production varies based on race [3] which can be explained by the presence of genes that alter cortisol production. Individuals who produce a lot of cortisol in response to inflammation have a tendency to develop a Cushingoid like response that includes obesity, type 2 diabetes/insulin resistance, hypertension, and dyslipidemia which is called metabolic syndrome.

Evidence that vaccines cause type 1 diabetes has been well established. Data from a large prospective clinical trial of the Haemophilus vaccine [4] as well as epidemiology data [5] support vaccines as a major causative agent for type 1 diabetes. The data from the clinical trial validates an animal toxicity model [4]. The findings were verified by others [6]. Discontinuation of vaccines has been repeatedly shown to be followed by declines in the rates of type 1 diabetes [5,7]. Evidence that vaccines cause type 2 diabetes, obesity and metabolic syndrome has been reviewed recently [2]. Evidence includes the observation that the discontinuation of school age BCG vaccination in Japan was followed by a decrease in type 2 diabetes in children in Japan [8].

Since 1999 the routine pediatric immunization schedule [9,10] increased by 80 vaccines. This number is derived by the fact that multivalent vaccines contain specific vaccines to each separate strain. The following have been added, pneumococcus (13 valent),

meningococcus (4 valent), human papilloma virus (4 valent), hepatitis A (1 valent), rotavirus (4 additional valent), influenza (3 valent per year x 18 years=54).

Disconnect between the Acceleration Diabetes Epidemic and the Stabilization of the Prevalence of Obesity

The theory of vaccine induced immune overload explains the acceleration of the diabetes epidemic at a time when the obesity epidemic has stopped. Data from the United States shows that the epidemic of obesity in children 12-19 has ended [11] however during a time when there was no increase in obesity in children age 12-19 the rates of prediabetes or diabetes increased from 9% to 23%. According to an alternate hypothesis, obesity was causing the diabetes epidemic and one would expect no increase in diabetes or prediabetes when the rates of obesity were constant. However the theory of vaccine induced immune over load explains the observation. According to the theory the obesity epidemic was caused by the physiological response to immune stimulation and the resulting cortisol production of the negative feedback loop of the immune system [2,3,12,13]. As the number of vaccines increased the negative feedback loop reached its maximum and the obesity rates stabilized. At that point additional vaccine induced immune stimulation was not met by an increase in negative feedback and the epidemic of diabetes (inflammation induced islet cell damage) increased.

Disconnect between Epidemics of Diabetes and other Components of Metabolic Syndrome

As discussed above, data on children age 12-19 showed the rates of obesity went from 18% to 20% (not statistically significant) while diabetes/prediabetes went from 9% to 23% in the years 1999-2000 to 2007-2008 [11]. During this time frame other components of metabolic syndrome experienced no increases. There was no increase in hypertension or decreases in HDL. LDL levels also did not rise. These findings can be explained by the vaccine induced immune overload theory. The negative feedback loop comprising cortisol production reached its maximum and further immune stimulation lead to immune destruction of islet cells, similar to what occurs in type 1 diabetes, without rises in symptoms consistent with increased cortisol production, obesity, hypertension, dyslipidemia.

Type 1.5 Diabetes in Children, Double Diabetes

There has been a recent increase in the diagnosis of children with features of both type 1 and type 2 diabetes [14] a condition called double diabetes or type 1.5 diabetes. This condition is new. A similar condition is being diagnosed much more frequently in adults as well and is called LADA, latent autoimmune diabetes in adults, as well as type 1.5 diabetes. The theory of immune overload explains the increasing prevalence of this condition. Under conditions of low vaccination and low immune stimulation, those who develop autoimmune type 1 diabetes include those with a low cortisol response to inflammation, while those who develop type II diabetes/metabolic syndrome include those which have a very high cortisol response to inflammation [3]. As the increasing number of vaccines increases inflammation those with a moderate cortisol response to inflammation develop diabetes. In persons with a moderate cortisol response, the individuals do not produce enough cortisol to prevent inflammation induced destruction of islet cells, type 1 diabetes, however they make

enough cortisol to develop insulin resistance and symptoms of type 2 diabetes.

Decreasing Importance of High risk MHC in Developing Type 1 Diabetes

It has been shown that with progression of time and the increase in the epidemic of type 1 diabetes that the proportion of children with high risk MHC genotypes for type 1 diabetes is decreasing [15]. This can be explained by vaccine induced immune overload. When the underlying level of inflammation in the population is low, those with high risk genes are more likely to develop type 1 diabetes. In an environment where the underlying level of inflammation in the population is elevated, because of extensive immunization, high risk MHC genotypes are less important to the development of the disease because elevated cytokines and activated immune cells are the key drivers of the disease.

Epidemic of NASH

NASH is a relatively new disease and was first described in 1979-1980 and is a type of fatty liver disease. NASH was shown to afflict 3% of children [16] in an autopsy study of children who died from 1993 to 2003. The study indicated fatty liver disease was found in 38% of obese children but was found in 5% of normal weight children. A recent paper indicated the percent of children aged 12-19 with elevated liver enzymes, specifically alanine aminotransferase levels, increased from 3.9% to 10.7% from 1988-1994 to 2007-2010 [17]. While there have been no direct epidemiology studies between NASH and vaccines, this epidemic can be explained by the rise in vaccine induced inflammation and vaccine induced diabetes. NASH is considered caused by multiple hits. One predisposing factor is the diabetes which as explained above is caused by vaccines. Another hit is cytokines [18] which are also caused by vaccine induced inflammation [2].

Parallel Epidemics of Inflammatory Diseases

The theory of vaccine induced immune overload explains the parallel epidemics of multiple different autoimmune diseases. It is a known fact that the pathophysiology is shared in many autoimmune and inflammatory diseases. Patients with autoimmune disease often have more than one autoimmune disease or have a family history of multiple different autoimmune diseases. It is thus not surprising that many inflammatory diseases are increasing along with type 1 diabetes, in fact it is expected. A wide variety of diseases have been reported to increasing in children. There are insufficient data to know if the prevalence of the majority of inflammatory diseases is increasing. However given the number and variety diseases that are reported to be increasing in children it is likely many more also increasing.

Epidemiology studies show a close linkage between type 1 diabetes and other autoimmune diseases. Type 1 diabetes is strongly linked with other autoimmune diseases in Type II polyglandular autoimmune syndrome [19]. In this syndrome 52% of patients have diabetes mellitus, 69% have autoimmune thyroid disease and 100% have Addison's disease. Patients with type 1 diabetes and their close relatives are at increased risk for organ specific autoimmune disease [20]. Some of the epidemiology data comes from studies of families where several members have autoimmune disease. Family studies indicate type 1 diabetes is linked to the development of several different autoimmune diseases including organ specific autoimmune

diseases and rheumatoid diseases. Close relatives of patients with type 1 diabetes have an increased risk of a wide variety of different autoantibodies [21,22]. It has been found that depending on the family, type 1 diabetes is linked with either an increased risk of an organ specific autoimmune disease or a rheumatoid disease [23]. A large study of Mennonites showed a linkage between type 1 diabetes and other autoimmune diseases including organ specific and rheumatoid diseases [24].

Immune stimulation with alpha interferon increases the risk of type 1 diabetes and a wide variety of other autoimmune diseases. People receive alpha interferon for the treatment of viral hepatitis and cancers. Alpha interferon has been repeatedly reported to cause type 1 diabetes in humans [25-28]. One of 40 patients receiving alpha interferon in a Japanese study developed anti-islet cell antibodies [28]. An Italian study found 14 of 11,241 patients receiving alpha interferon developed diabetes mellitus [29]. Alpha interferon also increases the risk of organ specific autoimmune diseases such as thyroiditis and autoimmune rheumatic diseases such as SLE, rheumatoid arthritis, psoriasis and sarcoid [30]. It has been reported that upon the administration of alpha interferon that the same patient developed both rheumatoid and organ specific autoimmune diseases [31,32].

It is well accepted that the diagnosis of autism is epidemic. Many cases of autism have a strong inflammatory component and the epidemic has already been linked to vaccine induced overload [33]. Autism epidemiological linked to diabetes and those with autism have a family history of increased risk for autoimmune diseases. Attention deficit syndrome is epidemic and epidemiological linked to increased risk of immune disorders [34].

Many inflammatory mediated diseases other than diabetes are epidemic. The incidence of psoriasis has been reported to double in children [35]. Autoimmune anti-neutrophil cytoplasmic antibody vasculitis resulting in renal failure has also been increased [36]. Wegener's Granulomatosis has been reported to increase in children [37]. The incidence of inflammatory bowel disease is also increasing rapidly in children [38].

Data indicates vaccines can act to sensitize recipients to environmental antigens. The CDC [39] found several vaccines were associated with an increased risk of asthma including the Haemophilus influenzae type b, relative risk 1.18 (1.02 to 1.36) and hepatitis B vaccine 1.20 (1.13 to 1.27). It is not surprising then that there is a rise in food related allergens [40]. Peanut allergy has tripled in children since 1997 [41]. Immune mediated food related disease, celiac disease [42], has also increased substantially.

Conclusion

There has been an epidemic of inflammatory diseases that has paralleled the epidemic on iatrogenic immune stimulation with vaccines. The epidemic of diabetes/prediabetes appears to be accelerating at a time when the prevalence of obesity has stabilized, indicating that the negative feedback system of the immune system has been over whelmed. The theory of vaccine induced immune overload explains the key observations that have confounded many competing hypothesis. Unfortunately the prospective controlled trials of vaccines performed for licensure are either too small, too short in duration or inappropriately controlled (use other vaccines as controls) to appropriately study the relationship between vaccines and these epidemics. Furthermore most epidemiological studies performed after licensure of vaccines suffer from the same deficiencies. The

conclusions of this paper are based on data from a single clinical trial, animal toxicity studies, and epidemiological studies. While it would be ideal to have more clinical trial data, industry and government have been reluctant to provide such information. However, conclusions regarding toxicity of many agents including cigarettes and asbestos were made without clinical trial data. The author believes that the sum of the data described and reviewed in this paper supports a casual relationship.

Acknowledgements/Conflicts

The author has patents pertaining to methods of testing vaccines for their ability to cause diabetes and methods of preventing diabetes.

References

1. Classen JB (1998) Method and Composition for an Early Vaccine to Protect Against Both Common Infectious Diseases and Chronic Immune Mediated Disorders or Their Sequelae. USA Patent 5723283.
2. Classen JB (2012) Review of evidence that epidemics of type 1 diabetes and type 2 diabetes/metabolic syndrome are polar opposite responses to iatrogenic inflammation. *Curr Diabetes Rev* 8: 413-418.
3. Classen JB (2009) Evidence childhood epidemics of type 1 and type 2 diabetes are opposite extremes of an immune spectrum disorder induced by immune stimulants. Role of race and associated cortisol activity as a major determining factor of diabetes. *Diabetes Metabol Syn Clin Res Rev* 3: 67-69.
4. Classen JB, Classen DC (2002) Clustering of cases of insulin dependent diabetes (IDDM) occurring three years after hemophilus influenza B (HiB) immunization support causal relationship between immunization and IDDM. *Autoimmunity* 35: 247-253.
5. Classen JB (2008) Risk of vaccine induced diabetes in children with a family history of type 1 diabetes. *Open Pediatr Med J* 2: 7-10.
6. Wahlberg J, Fredriksson J, Vaarala O, Ludvigsson J; Abis Study Group (2003) Vaccinations may induce diabetes-related autoantibodies in one-year-old children. *Ann N Y Acad Sci* 1005: 404-408.
7. Classen JB, Classen DC (2003) Clustering of cases of type 1 diabetes mellitus occurring 2-4 years after vaccination is consistent with clustering after infections and progression to type 1 diabetes mellitus in autoantibody positive individuals. *J Pediatr Endocrinol Metab* 16: 495-508.
8. Classen JB (2008) Discontinuation of BCG vaccination precedes significant drop in type 2 diabetes in Japanese children. Role of inflammation and cortisol activity as a cause of type 2 diabetes. *Open Endocrinol J* 2: 1-4.
9. [No authors listed] (1999) Recommended childhood immunization schedule-United States, January-December 1999. American Academy of Pediatrics Committee on Infectious Diseases. *Pediatrics* 103: 182-185.
10. Centers for Disease Control and Prevention (CDC) (2013) Advisory Committee on Immunization Practices (ACIP) recommended immunization schedules for persons aged 0 through 18 years and adults aged 19 years and older--United States, 2013. *MMWR Surveill Summ* 62 Suppl 1: 1.
11. May AL, Kuklina EV, Yoon PW (2012) Prevalence of cardiovascular disease risk factors among US adolescents, 1999-2008. *Pediatrics* 129: 1035-1041.
12. Classen JB (2011) Italian pediatric data support hypothesis that simultaneous epidemics of type 1 diabetes and type 2 diabetes/metabolic syndrome/obesity are polar opposite responses (i.e symptoms) to a primary inflammatory condition. *JPEM* 24: 455-456.
13. Classen JB (2008) Type 1 versus type 2 diabetes/metabolic syndrome, opposite extremes of an immune spectrum disorder induced by vaccines. *Open Endocrinol J* 2: 9-15.

14. Pozzilli P, Guglielmi C, Caprio S, Buzzetti R (2011) Obesity, autoimmunity, and double diabetes in youth. *Diabetes Care* 34 Suppl 2: S166-170.
15. Vehik K, Hamman RF, Lezotte D, Norris JM, Klingensmith GJ, et al. (2008) Trends in high-risk HLA susceptibility genes among Colorado youth with type 1 diabetes. *Diabetes Care* 31: 1392-1396.
16. Schwimmer JB1, Deutsch R, Kahen T, Lavine JE, Stanley C, et al. (2006) Prevalence of fatty liver in children and adolescents. *Pediatrics* 118: 1388-1393.
17. Welsh JA, Karpen S, Vos MB (2013) Increasing prevalence of nonalcoholic fatty liver disease among United States adolescents, 1988-1994 to 2007-2010. *J Pediatr* 162: 496-500.
18. Tilg H, Diehl AM (2000) Cytokines in alcoholic and nonalcoholic steatohepatitis. *N Engl J Med* 343: 1467-1476.
19. Trencle DL, Morley JE, Handwerker BS (1984) Polyglandular autoimmune syndromes. *Am J Med* 77: 107-116.
20. Batterle C, Zanette F, Pedini B, Presotto F, Rapp LB, et al. (1984) Clinical and subclinical organ specific autoimmune manifestations in type 1 (insulin dependent) diabetic patients and their first degree relatives. *Diabetologia* 26: 431-436.
21. Hagglof B, Rabinovitch A, Mackay P, Huen A, Rubenstein AH, et al. (1986) Islet cell and other organ-specific autoantibodies in healthy first-degree relatives to insulin-dependent. *Acta Paediatr Scand* 75: 611-618.
22. Lorini R, Larizza D, Livieri C, Cammareri V, Martini A, et al. (1986) Auto-immunity in children with diabetes mellitus and in their relatives. *Eur J Pediatr* 145: 182-184.
23. Torfs CP, King MC, Huey B, Malmgren J, Grumet FC (1986) Genetic interrelationship between insulin dependent diabetes mellitus, the autoimmune thyroid diseases, and rheumatoid arthritis. *Am J Hum Genet* 38: 170-187.
24. Jaworski MA, Severini A, Mansour G, Hennig K, Slater JD, et al. (1989) Inherited diseases in North American Mennonites: focus on Old Colony (Chortitza) Mennonites. *Am J Med Genet* 32: 158-168.
25. Waguri M, Hanafusa T, Itoh N, Imagawa A, Miyagawa J, et al. (1994) Occurrence of IDDM during interferon therapy for chronic viral hepatitis. *Diabetes Res Clin Pract* 23: 33-36.
26. Murakami M, Iriuchijima T, Mori M (1995) Diabetes mellitus and interferon-alpha therapy. *Ann Intern Med* 123: 318.
27. Fabris P, Betterle C, Floreani A, Greggio NA, de Lazzari F, et al. (1992) Development of type 1 diabetes mellitus during interferon alfa therapy for chronic HCV hepatitis. *Lancet* 340: 548.
28. Imagawa A, Itoh N, Hanafusa T, Waguri M, Kuwajima M, et al. (1996) Antibodies to glutamic acid decarboxylase induced by interferon-alpha therapy for chronic viral hepatitis. *Diabetologia* 39: 126.
29. Fattovich G, Giustina G, Favarato S, Ruol A (1996) A survey of adverse events in 11,241 patients with chronic viral hepatitis treated with alpha interferon. *J Hepatol* 24: 38-47.
30. Neshler G, Ruchlemer R (1998) Alpha-interferon-induced arthritis: clinical presentation treatment, and prevention. *Semin Arthritis Rheum* 27: 360-365.
31. Pittau E, Bogliolo A, Tinti A, Mela Q, Ibba G, et al. (1997) Development of arthritis and hypothyroidism during alpha-interferon therapy for chronic hepatitis C. *Clin Exp Rheumatol* 15: 415-419.
32. D'Hondt L, Delannoy A, Docquier C (1993) Hypothyroidism and arthritis during interferon therapy. *Clin Rheumatol* 12: 415-417.
33. Classen JB (2013) Prevalence of Autism is Positively Associated with the Incidence of Type 1 Diabetes, but Negatively Associated with the Incidence of Type 2 Diabetes, Implication for the Etiology of the Autism Epidemic. *Open Access Sci Rep* 2: 1-3.
34. Chen MH, Su TP, Chen YS, Hsu JW, Huang KL, et al. (2013) Comorbidity of Allergic and Autoimmune Diseases Among Patients with ADHD: A Nationwide Population-Based Study. *J Atten Disord*.
35. Tollefson MM, Crowson CS, McEvoy MT, Maradit Kremers H (2010) Incidence of psoriasis in children: a population-based study. *J Am Acad Dermatol* 62: 979-987.
36. Sethna C, Frank R, Infante L, Gottlieb B, Eberhard A, et al. (2012) Anti-Neutrophil Cytoplasmic Antibody Vasculitis in Pediatric Patients: Is the Incidence Rising? *Open J Nephrol* 2: 19-22.
37. Grisaru S, Yuen GW, Miettunen PM, Hamiwka LA (2010) Incidence of Wegener's granulomatosis in children. *J Rheumatol* 37: 440-442.
38. Lehtinen P, Ashorn M, Iltanen S, Jauhola R, Jauhonen P, et al. (2011) Incidence trends of pediatric inflammatory bowel disease in Finland, 1987-2003, a nationwide study. *Inflamm Bowel Dis* 17: 1778-1783.
39. DeStefano F, Gu D, Kramarz P, Truman BI, Iademaro MF, et al. (2002) Childhood vaccinations and risk of asthma. *Pediatr Infect Dis J* 21: 498-504.
40. Prescott S, Allen KJ (2011) Food allergy: riding the second wave of the allergy epidemic. *Pediatr Allergy Immunol* 22: 155-160.
41. Sicherer SH, Muñoz-Furlong A, Godbold JH, Sampson HA (2010) US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol* 125: 1322-1326.
42. Dydensborg S, Toftedal P, Biaggi M, Lillevang ST, Hansen DG, et al. (2012) Increasing prevalence of coeliac disease in Denmark: a linkage study combining national registries. *Acta Paediatr* 101: 179-184.

This article was originally published in a special issue, entitled: "**Molecular and Cellular Aspects in Obesity and Diabetes**", Edited by Dr. Masayoshi Yamaguchi, Emory University School of Medicine, USA