Correlation of type 1 diabetes trends in European countries to the number of bovine insulin and GAD65 contaminated chick embryo cell culture containing vaccines in the schedule, as predicted by the autoimmunity mechanism involving immunization with homologous xenogeneic antigens and EPIT as a potential treatment

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Abstract

Type 1 diabetes (T1D) affects millions and is a growing problem worldwide. The etiology of T1D is considered to be unknown.

Many vaccines are manufactured using bovine milk derived proteins such as bovine casein and casamino acids as growth media to grow bacteria. These vaccines contain trace quantities of all bovine milk proteins.

Similarly, other vaccines are manufactured using animal cells such as chick embryo cell culture, to grow viruses. These vaccines contain trace quantities of chick embryo proteins.

Such non-target protein content in vaccines are not regulated. No safe levels of such proteins in vaccines have been determined. There are no specifications controlling the amount of such proteins in vaccines. A recent example is the case of Pandemrix induced narcolepsy, where Arepanrix and Pandemrix vaccines made by the same vendor, GSK, at two different facilities, contained differing amounts of H1N1 nucleoproteins thus resulting in a big difference in the incidence of vaccine-induced narcolepsy. The safety claims of such vaccines are based on studies that misinterpret the statistics and have therefore come to the wrong conclusion regarding safety.

Animal proteins have molecular mimicry to human proteins. Therefore immune responses generated against animal proteins can result in cross reaction to human proteins. The result is autoimmune disorders such as type 1 diabetes (T1D).

The trends and cyclical variation of type 1 diabetes incidence in European countries was recently described. The cyclical variation can be explained by the interval between vaccine doses. Positive correlation is shown between the number of milk protein and chick embryo cell culture containing vaccines on the schedule and the rate of increase in T1D.

Introduction

Type 1 diabetes (T1D) affects millions and is a growing problem worldwide. The etiology of T1D is considered to be unknown.

Many vaccines are manufactured using bovine milk derived proteins such as bovine casein and casamino acids as growth media to grow bacteria.(1) These vaccines contain trace quantities of all bovine milk proteins.(2)

Similarly, other vaccines are manufactured using animal cells such as chick embryo cell culture to grow viruses. These vaccines contain trace quantities of chick embryo proteins.

Animal proteins have molecular mimicry to human proteins. Therefore immune responses generated against animal proteins can result in cross reaction to human proteins. The result is autoimmune disorders such as type 1 diabetes (T1D).

Patterson et al.(3) describe the trends and cyclical variation of type 1 diabetes incidence in European countries.

Discussion

Cyclical pattern

Epidemiological studies of vaccines and T1D misinterpret the statistics thus resulting in type 2 errors. (4,5)

It is easy to show that two vaccine doses separated by 4 years will result in a 4 year cyclical variation of incidence. However, there are numerous autoantigens involved in T1D. For example, chick GAD65 protein containing chick embryo cell culture derived measles, mumps, rubella (MMR)(6) and tick borne encephalitis (TBE) vaccines can cause GAD65 related T1D due to molecular mimicry and cross reaction to human GAD65.(7) Bovine milk protein containing vaccines such as diphtheria, tetanus, acellular pertussis (DTaP)(8), pneumococcal vaccine (PCV), haemophilus influenzae B (Hib) (1) contain bovine insulin(9) which similarly induce an autoimmune response against human insulin secreting cells.(10) The autoimmune responses can be humoral and cell mediated.

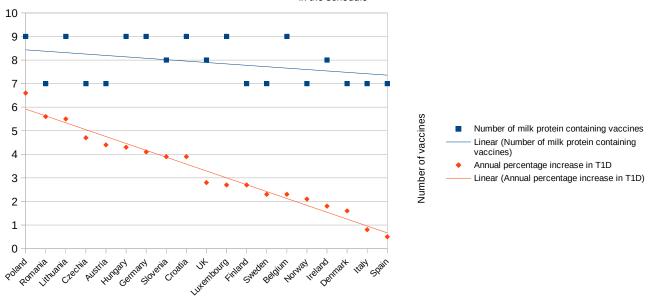
Therefore cyclical variation can be expected but it will likely be a function involving multiple sinusoids of differing frequencies and amplitudes. Genetic susceptibility to a specific autoantigen related T1D will also vary by region. There is no regulation or specification that controls the level of animal protein contamination of vaccines.(11,12) As we found in the case of Pandemrix induced narcolepsy, Arepanrix and Pandemrix vaccines made by the same vendor, GSK, at two different facilities, contained differing amounts of H1N1 nucleoproteins, thus resulting in a big difference in the incidence of vaccine-induced narcolepsy.(13–15)

These factors need to be accounted in trying to explain the pattern of T1D incidence.

The mechanisms by which immunization with homologous xenogeneic antigen (animal protein) containing vaccines result in abrogation of peripheral tolerance was previously described.(16,17)

Correlation to number of vaccines

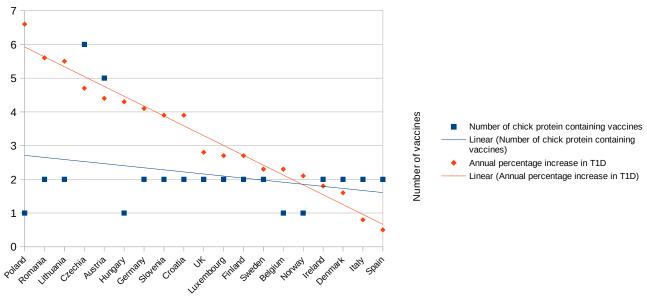
The vaccine schedules in various European countries differ in the number of DTaP, Hib, TBE and MMR vaccines recommended in the first 7 years of life.(18) The number of PCV vaccine doses in the schedules were the same and was therefore not included in this analysis. Correlation between number of vaccines and annual percentage increase in T1D are shown below. The country specific T1D percent increase data was obtained from the ESM 3 Table of the supplementary material provided by Patterson et al.(3)



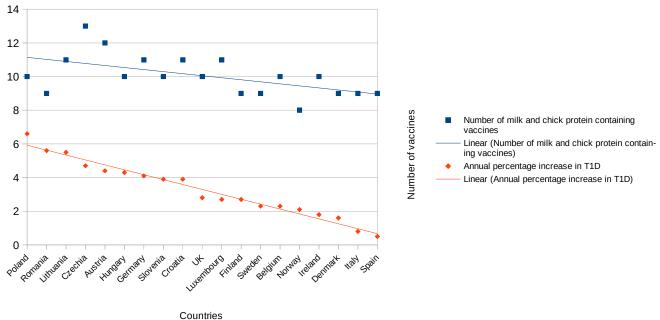
Correlation of annual percentage increase in T1D to the number of bovine insulin containing vaccine doses in the schedule

Countries

Correlation of annual percentage increase in T1D to the number of GAD65 contaminated chick embryo cell culture containing vaccine doses in the schedule



Countries



Correlation of annual percentage increase in T1D to the number of bovine insulin and GAD65 contaminated chick embryo cell culture containing vaccine doses in the schedule

Conclusion

The solution to this problem is the immediate removal of all non-target proteins from vaccines by using processes such as affinity chromatography.(19)

Epicutaneous immunotherapy (EPIT) could be a potential prevention or treatment for indivduals exposed to such animal protein containing vaccines. Topical chicken protein to treat T1D was previously described.(20) The expected effect is similar to a decrease in incidence of T1D reported using EPIT on non obese diabetic mice.(21)

Also similarly, topical bovine milk protein may help prevent or treat T1D. A milk-free diet may also help prevent or treat T1D involving IgG4 mediated disease.(10)

References

- 1. Vaccine Excipient & Media Summary [Internet]. 2015 [cited 2016 Jan 16]. Available from: http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf
- 2. Kattan JD, Cox AL, Nowak-Wegrzyn A, Gimenez G, Bardina L, Sampson HA, et al. Allergic reactions to diphtheria, tetanus, and acellular pertussis vaccines among children with milk allergy. J Allergy Clin Immunol. 2011;Conference(var.pagings):AB238.

- 3. Patterson CC, Harjutsalo V, Rosenbauer J, Neu A, Cinek O, Skrivarhaug T, et al. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989–2013: a multicentre prospective registration study. Diabetologia. 2018;
- 4. Arumugham V. MMR, TBE vaccine and type 1 diabetes [Internet]. The BMJ. 2018. Available from: https://www.bmj.com/content/360/bmj.k1378/rr-2
- 5. Ioannidis JPA. Why most published research findings are false. PLoS Med. 2005/08/30 ed. Public Library of Science; 2005 Aug;2(8):e124–e124.
- 6. MMR II Vaccine Package Insert [Internet]. [cited 2016 May 3]. Available from: http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ UCM123789.pdf
- Arumugham V. Role of MMR II vaccine contamination with GAD65 containing chick embryo cell culture in the etiology of type 1 diabetes [Internet]. 2017. Available from: https://www.zenodo.org/record/1034771
- 8. Glaxo Smith Kline. Infanrix package insert [Internet]. Available from: https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ ucm124514.pdf
- 9. Aranda P, Sanchez L, Perez MD, Ena JM, Calvo M. Insulin in bovine colostrum and milk: evolution throughout lactation and binding to caseins. J Dairy Sci. United States; 1991 Dec;74(12):4320–5.
- 10. Arumugham V. Milk containing vaccines cause milk allergies, EoE, autism and type 1 diabetes [Internet]. The BMJ. 2018. Available from: https://www.bmj.com/content/361/bmj.k2396/rr
- 11. Arumugham V. Evidence that Food Proteins in Vaccines Cause the Development of Food Allergies and Its Implications for Vaccine Policy. J Dev Drugs. 2015;4(137):2.
- National Academies of Sciences and Medicine E. Finding a Path to Safety in Food Allergy: Assessment of the Global Burden, Causes, Prevention, Management, and Public Policy. Stallings VA, Oria MP, editors. Washington, DC: The National Academies Press; 2017.
- Arumugham V. Pharmacovigilance is no substitute for good vaccine design [Internet]. The BMJ.
 2018. Available from: https://www.bmj.com/content/362/bmj.k3948/rr-11
- Arumugham V. Pandemrix and Arepanrix vaccine safety analysis and scrutiny fell short [Internet]. The BMJ. 2018. Available from: https://www.bmj.com/content/363/bmj.k4152/rr-14
- 15. Ahmed SS, Volkmuth W, Duca J, Corti L, Pallaoro M, Pezzicoli A, et al. Antibodies to influenza nucleoprotein cross-react with human hypocretin receptor 2 (ABSTRACT ONLY). Sci Transl Med. 2015;7(294):294ra105–294ra105.

- 16. Arumugham V, Trushin M V. Cancer immunology, bioinformatics and chemokine evidence link vaccines contaminated with animal proteins to autoimmune disease: a detailed look at Crohn's disease and Vitiligo. J Pharm Sci Res. 2018;10(8):2106.
- 17. Arumugham V. Bioinformatics analysis links type 1 diabetes to vaccines contaminated with animal proteins and autoreactive T cells express skin homing receptors consistent with injected vaccines as causal agent [Internet]. 2017. Available from: https://www.zenodo.org/record/1034775
- 18. ECDC. Vaccine Scheduler [Internet]. Available from: https://vaccine-schedule.ecdc.europa.eu
- 19. Zhao M, Vandersluis M, Stout J, Haupts U, Sanders M, Jacquemart R. Affinity chromatography for vaccines manufacturing: Finally ready for prime time? Vaccine. Netherlands; 2018 Apr;
- 20. Arumugham V. Topical chicken protein to treat type 1 diabetes? The immunological basis explained ... [Internet]. 2017. Available from: https://www.zenodo.org/record/1034781
- 21. Dupont CM, Pelletier B, Dhelft V, Ligouis M, Sampson HA, Benhamou P-H, et al. EPIT decreases T1D incidence in sensitized non obese diabetic mice: a likely bystander effect of EPIT-induced Tregs. J Allergy Clin Immunol. Elsevier; 2018 Apr 21;139(2):AB16.