PACIFIC HEALTH DIALOG
MARCH 2014 · VOLUME 20 · NUMBER 1

ANALYSIS

Rheumatic Fever in New Zealand: what are the teeth trying to tell us?

Thornley S, Sundborn G, Schmidt-Uili S M.

ABSTRACT

Rheumatic fever remains an important disease of childhood in New Zealand, despite increasing access and awareness of the need for preventive antibiotic treatment. Māori and Pacific children have an incidence rate about 30 times and 70 times higher than European children, from annual notification data (77.7 per 100,000 for Pacific, 30.4 per 100,000 for Māori, and 1 per 100,000 for European). In the early 20th century, a Canadian dentist, Weston A. Price, noted that 95% of children who presented with acute rheumatic fever also had advanced dental caries. Oral health surveys show that Māori and Pacific children are disproportionately affected by dental caries compared to European. Excess dietary sugar intake is widely recognised to cause dental decay and also provides energy to some species of bacteria implicated in the pathogenesis of dental decay and rheumatic fever. We suggest that a case-control study be conducted to evaluate the evidence for an association between sugar intake, dental decay and incidence of disease.

COMPETING INTERESTS: Nil

AUTHOR INFORMATION:

Simon Thornley, Public Health Physician;
Gerhard Sundborn, Post-Doctoral Fellow,
Seinafolava Meia Schmidt-Uili, General Paediatrician.

CORRESPONDENCE:

Simon Thornley, Public Health Physician, The University of Auckland, Level 4, School of Population Health, Tamaki Innovation Campus, Private Bag 92019, Auckland 1142. Phone: +64 9 3737599 ext.86722, fax: +64 9 3737503, email: s.thornley@auckland.ac.nz

FUNDING:

Simon Thornley is funded by an HRC Clinical Research Training Fellowship (HRC ref: 11/145) and Gerhard Sundborn is funded by an HRC Pacific Health Research Postdoctoral Fellowship.

The epidemiology of rheumatic fever in New Zealand intrigues us. It is a disease of childhood almost absent from many Western nations,[1] however, in New Zealand, children continue to suffer from the condition and its sequelae. Why? Here, we consider the evidence that a component of the diet of children, sugar, explains some of the epidemiological trends associated with the disease.

The onset of acute rheumatic fever is often associated with group A streptococcal infection in the upper respiratory tract, with the systemic, joint and cardiac involvement thought to represent an auto-immune response to the infection.[2] Since the 1960s, cross-reactivity has been demonstrated between Group A beta haemolytic streptococci and human heart tissue.[3] An M-protein has isolated in these bacteria cross-reacts with cardiac myosin, which results in a T-cell mediated inflammatory reaction, following infection with the organism.[4,5] This molecular mimicry explains the link between infection with group A beta haemolytic streptococci and the cardiac inflammation associated with rheumatic fever.

In New Zealand, the burden of disease shows striking differences by ethnic group.[6] Mostly, acute rheumatic fever occurs in Māori and Pacific populations. The age-specific annual notification rates for acute rheumatic fever between 1990 and 1995 for children aged 10 to 14 years was 77.7 per 100,000 for Pacific children, 30.4 per 100,000 for Māori, and 1 per 100,000 for European.[7] This represents an extraordinarily difference. The New Zealand Guidelines for the disease explain that no genetic differences, to date, explain this variation, and that the varied

burden "reflects social, political, and economic influences that result in overcrowded conditions, socioeconomic deprivation, an increased incidence of upper respiratory infections with GAS [group A streptococcal infections], and different options or opportunities for appropriate and effective health care."[8] Here, we argue that the sugar intake, observed through differences in the prevalence of tooth decay, may explain some of the ethnic differences in the incidence of disease.

Group A streptococcal infections also cause other infections including cellulitis, erysipelas, impetigo and glomerulonephritis. An analysis of a case-series of such patients in the Auckland region showed marked differences with population incidence of 21.6 per 100,000/ two years in Māori, 19.3 in Pacific and 5.3 in other ethnic groups.[9] The epidemiology of skin infection follows a similar pattern with a population study from South Auckland estimating that Māori and Pacific children (aged 1 to 14 years) were at nearly four times the risk of admission for skin infection of the limbs, compared to other ethnic groups (relative risk 3.89; 95% CI: 2.33 to 6.52).[10]

Antibiotics are often used to treat streptococcal throat infections, to prevent the onset of rheumatic fever. This has prompted campaigns, past and on-going, to enhance access to treatment. One example is through the use of school-based clinics. Do they work? One would expect so, but the results of a large cluster-randomised study, conducted in New Zealand, however, were disappointing. In the first analysis, after almost 87,000 person years of follow-up, 55/100,000 cases occurred in the clinic schools compared to 67/100,000 in the non-clinic schools, a difference that was not statistically significant.

What other approaches to prevention may be considered? In a book originally published in 1938, written by a Canadian Dentist, a clue may be found.[11] Weston A. Price investigated the prevalence of dental caries among indigenous populations who were eating traditional diets, comparing to those eating mainly Western foods. He made detailed written and photographic records of facial and dental abnormalities absent from those eating traditional diets, but present with increasing frequency with exposure to the Western diet. Often, the new foodstuffs consisted of sugar, white flour, and tinned foods. To a varying extent, these new items displaced the traditional diet.

Price reflects that "My studies have shown that in about 95% of these cases [acute rheumatic fever and bacterial endocarditis] there is active tooth decay".[11] To him the association between dental caries and rheumatic fever was unmistakeable, yet, to our knowledge, not a single published scientific article describes this association, from searching online databases. One article discusses the high prevalence of dental caries among indigenous Australian communities, and also discusses the high prevalence of rheumatic fever in the same populations, but draws no aetiological connection between the two conditions.[12] One case-control study, conducted in Bangladesh, shows an association between rheumatic fever and serum indices of iron deficiency and malnutrition (low haemoglobin and haematinics and low serum albumin. The study also links low HDL-cholesterol with disease status, although this finding is not highlighted by the authors.[13] In studies of adults, low HDL-cholesterol has been associated with high sugar intake.[14]

The effects of sugar (sucrose) intake on the adult population have started to regain attention with large organisations, such as the American Heart Association, recommending severe restriction of intake of the substance, to prevent weight gain and protect cardiovascular health.[15,16] Dentists have long recognised that sugar intake is an important causal factor in dental decay. The British Nutrition Foundation summarised the evidence by stating "the evidence establishing sugars as an aetiological factor in dental caries is overwhelming. The foundation of this lies in the multiplicity of studies rather than the power of any one".[17] Other authors have suggested that starch and all fermentable carbohydrates play a role in dental decay,[18] but it is likely that sucrose intake is most important. This is useful, in that the dental caries may serve as an objective indicator of sugar exposure, given the inaccuracy associated with self-report of dietary intake, particularly among children.

Given the ethnic differences in incidence of acute rheumatic fever, if sugar intake contributes to disease, we would expect that dental decay would disproportionately affect Māori and Pacific children. The epidemiological data is consistent with this theory. For almost all oral health indicators, in a recent national survey, New Zealand children and adolescents, aged 2-17 indices of dental decay were worse for Māori and Pacific compared to European. For example, the prevalence of being caries free in all teeth was 52.1% (95% CI: 45.8 to 58.3) among European, 38.4% (95% CI: 32.6 to 44.1) in Māori and 35.6% (95% CI: 27.2 to 43.9) in Pacific peoples.[19] The pattern observed here with dental caries matches the rank order, according to ethnic group, in incidence of acute rheumatic fever.

The last New Zealand children's dietary survey,[20] conducted in 2002, showed a different pattern of variation in self-reported sucrose intake, by ethnic group, compared to the dental study. Among five and six year olds, boys generally consumed larger quantities than girls. Māori children reported the highest intakes (boys, mean 66g/day; girls 59g/day), followed by Pacific (boys, mean 57g/day; girls 48g/day) with Europeans reporting mean intakes of 55g/day for both girls and boys of that age range.[20] So, Māori boys stand out as, on average, report eating about three teaspoons of sugar more than all other gender and ethnicity categories. Little difference in intake was observed by socio-economic status. Since these subjective reports are affected by social desirability and recall bias, with one study estimating a 20% discrepancy between observed and reported sugar intakes,[21] we believe that dental examinations are likely to provide a more objective assessment of the rank order of sugar intake between ethnic groups.

From a biological perspective, sugar (sucrose) is a source of energy, metabolised by some group A streptococci.[22] Also, one of the group A strains (Streptococcus mutans) is known to play a central role in the pathogenesis of dental caries,[23] so that it is quite plausible that sugar intake and dental caries play a role in the development of acute rheumatic fever. While Streptococcus pyogenes is the bacterium most commonly associated with rheumatic fever, one study showed that, in rabbits, inoculation with cariogenic Streptococcus mutans bacteria also stimulates the release of heart-reactive antibody.[24] In an analogous fashion, the presence of antibodies to the fructose metabolising, cariogenic Porphyromonas gingivalis is associated with auto-antibody positivity in people at risk of rheumatoid arthritis.[25]

Our hypothesis is summarised in the figure. The lines indicate causal links between factors that may influence the development of disease. We speculate that ethnic differences in dietary practices lead to variation in sucrose intake, with higher intakes in Māori and Pacific children. The sugar then leads to dental caries, and provides a substrate for growth of the pathogenic bacteria. Increased probability of disease then results from these factors. This does not exclude the possible influence of other factors, for example, socioeconomic deprivation, overcrowding or access to healthcare, as other influences on disease aetiology. Not shown in the diagram is the likely influence of poverty, which is statistically linked to ethnic group.[26] From overseas studies, poverty is positively associated with added sugar intake in early childhood.[27] The weakest level of evidence in our theory is the anecdotal report of what was in effect a career case-series.

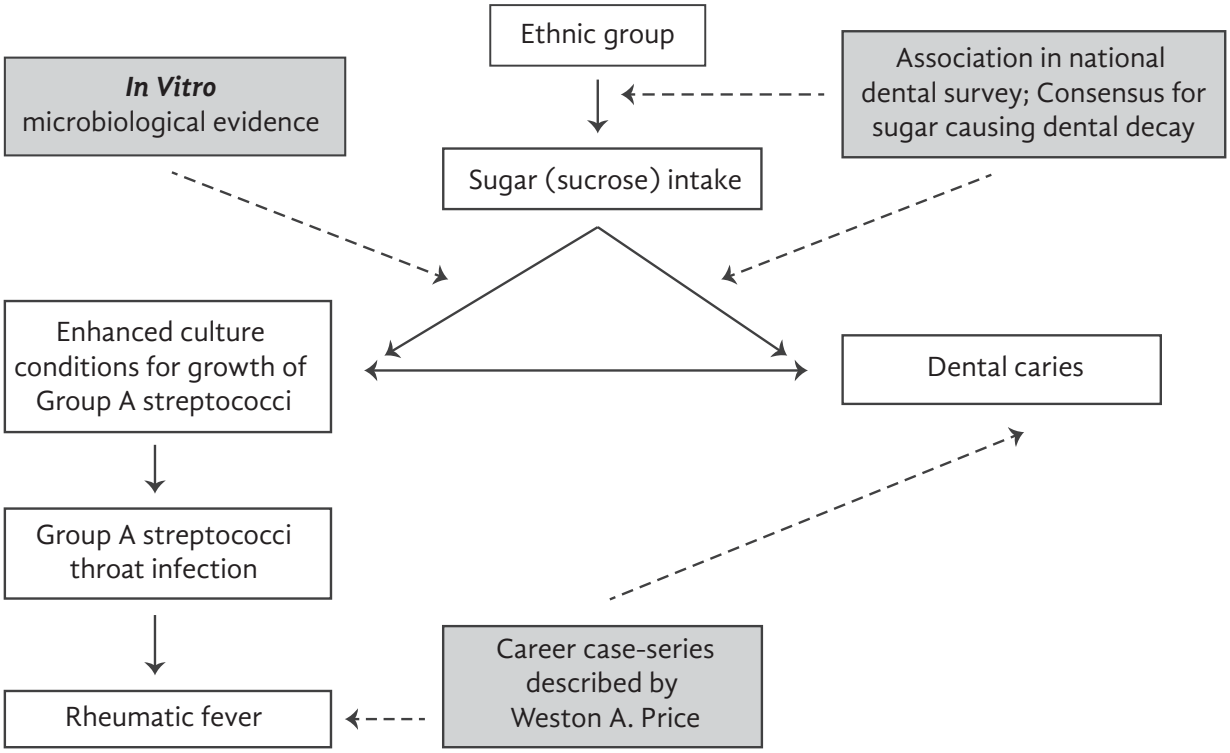

FIGURE. Proposed causal pathway which links sugar intake to the incidence of acute rheumatic fever. White boxes represent factors which may be on the causal pathway. Grey boxes show the nature of the evidence used to support the hypothesis.

Where to from here?

Given the rarity of acute rheumatic fever, a case-control study may be justified to look for associations between exposure (dental caries and sugar intake) and disease within individuals. In addition, in individuals with a history of the disease, avoiding sugar may reduce the incidence of relapse, and chronic rheumatic heart disease. If our theory proves correct, immediate changes to population nutrition policies, limiting sugar intake, and clinical treatment strategies along the same lines may be justified.

References

1. Seckeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clinical epidemiology 2011;3:67-84.

2. Rothman KJ, Greenland S, Walker AM. Concepts of interaction. Am. J. Epidemiol. 1980;112(4):467-70.

3. Kaplan MH, Frengley JD. Autoimmunity to the heart in cardiac disease. Current concepts of the relation of autoimmunity to rheumatic fever, postcardiotomyand postinfarction syndromes and cardiomyopathies. Am. J. Cardiol. 1969;24(4):459-73.

4. Guilherme L, Kalil J. Rheumatic Fever and Rheumatic Heart Disease: Cellular Mechanisms Leading Autoimmune Reactivity and Disease. J. Clin. Immunol. 2010;30(1):17-23.

5. Guilherme L, Ramasawmy R, Kalil J. Rheumatic fever and rheumatic heart disease: Genetics and pathogenesis. Scand. J. Immunol. 2007;66(2-3):199-207.

6. Wilson N. Rheumatic Heart Disease in Indigenous Populations—New Zealand Experience. Heart, Lung and Circulation 2010;19 (5-6):282-88.

7. Thornley C, McNicholas A, Baker M, Lennon D. Rheumatic fever registers in New Zealand. Public Health Report, 2001:41-4.

8. Atatoa-Carr P, Lennon D, Wilson N, New Zealand Rheumatic Fever Guidelines Writing G. Rheumatic fever diagnosis, management, and secondary prevention: a New Zealand guideline. N. Z. Med. J. 2008;121(1271):59-69.

9. Safar A, Lennon D, Stewart J, Trenholme A, Drinkovic D, Peat B. Invasive group A streptococcal infection and vaccine implications, Auckland, New Zealand, 2005–2006. . Emerg Infect Dis [serial on the Internet] 2011;Jun.

10. Finger F, Rossaak M, Umstaetter R, Reulbach U, Pitto R. Skin infections of the limbs of Polynesian children. N. Z. Med. J. 2004;117(1192):U847.

11. Price WA. Nutrition and physical degeneration: a comparison of primitive and modern diets and their effects (6th Edition). Keats Publishing, 2003.

12. Martin-Iverson N, Phatouros A, Tennant M. A brief review of indigenous Australian health as it impacts on oral health. Aust. Dent. J. 1999;44(2):88-92.

13. Zaman MM, Yoshiike N, Rouf MA, Haque S, Chowdhury AH, Nakayama T, et al. Association of rheumatic fever with serum albumin concentration and body iron stores in Bangladeshi children: case-control study. BMJ 1998;317(7168):1287-88.

14. Welsh JA, Sharma A, Abramson JL, Vaccarino V, Gillespie C, Vos MB. Caloric Sweetener Consumption and Dyslipidemia Among US Adults. JAMA: The Journal of the American Medical Association 2010;303(15):1490-97.

15. Johnson RK, Appel LJ, Brands M, Howard BV, Lefevre M, Lustig RH, et al. Dietary Sugars Intake and Cardiovascular Health: A Scientific Statement From the American Heart Association. Circulation 2009;120(11):1011-20.

16. Thornley S, Tayler R, Sikaris K. Sugar restriction: the evidence for a drug-free intervention to reduce cardiovascular disease risk. Intern. Med. J. 2012;42 Suppl 5:46-58.

17. Sheiham A. Dietary effects on dental diseases. Public Health Nutr. 2001;4(2b):569-91.

18. Hujoel P. Dietary Carbohydrates and Dental-Systemic Diseases. J. Dent. Res. 2009;88(6):490-502.

19. Ministry of Health. Our Oral Health: Key findings of the 2009 New Zealand Oral Health Survey. Wellington: Ministry of Health, 2010.

20. Ministry of Health. NZ Food NZ Children: Key results of the 2002 National Children's Nutrition Survey. Wellington: Ministry of Health, 2003.

21. Karvetti RL, Knuts LR. Validity of the 24-hour dietary recall. J. Am. Diet. Assoc. 1985;85(11):1437-42.

22. Chassy BM, Beall JR, Bielawski RM, Porter EV, Donkersloot JA. Occurrence and distribution of sucrose-metabolizing enzymes in oral streptococci. Infect. Immun. 1976;14(2):408-15.

23. Al-Dajani M, Limeback H. Emerging science in the dietary control and prevention of dental caries. J. Calif. Dent. Assoc. 2012;40(10):799-804.

24. Van de Rijn I, Bleiweis AS, Zabriskie JB. Antigens in Streptococcus mutans cross reactive with human heart muscle. J. Dent. Res. 1976;55 Spec No:C59-64.

25. Mikuls TR, Thiele GM, Deane KD, Payne JB, O'Dell JR, Yu F, et al. Porphyromonas gingivalis and disease-related autoantibodies in individuals at increased risk of rheumatoid arthritis. Arthritis Rheum. 2012;64(11):3522-30.

26. The Ministry of Social Development. 2010 the social report. Wellington: The Ministry of Social Development, 2011.

27. Kranz S, Siega-Riz AM. Sociodemographic determinants of added sugar intake in preschoolers 2 to 5 years old. The Journal of Pediatrics 2002;140(6):667-72.