

A specific hygiene hypothesis

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ABSTRACT

Allergic diseases have reached epidemic proportions in Western populations in the last several decades. The hygiene hypothesis proposed more than twenty years ago has helped us to understand the epidemic and has been verified with numerous studies. However, translational measures deduced from these studies to prevent allergic diseases have not proven effective. Recent studies on immigrants' allergies and any potential association between oral infection and allergic diseases prompt me to propose a specific hygiene hypothesis to explain how oral hygiene practices might have contributed to the uprising of hay fever, the most common allergic disease. The historic oral hygiene level in US is closely associated with the emerging allergic epidemic. Future studies to test the hypothesis are needed and verification of the hypothesis can potentially yield highly effective measures to prevent allergic diseases.

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Introduction

Allergies are a significant health concern. Allergic diseases have reached epidemic proportions in Western populations in the last decades. Hay fever (allergic rhinitis or seasonal allergy) is the most common allergic disease, affecting 13.5% of the US population [1]. Its symptoms include any combination of the following: a runny or stuffy nose, sneezing, itchy nose, red eyes, and congestion. The hygiene hypothesis was proposed by Strachan in 1989 to explain the cause [2], which is referred to here as general hygiene hypothesis (GHH). Since then, a variety of studies reported results consistent with GHH, including that rural farm living significantly reduces the risk of developing hay fever and atopic sensitization [3,4]. These environmental cues point to lack of access to microbial diversity as a possible cause of allergies and autoimmune diseases [5–8]. The observed link between allergy and commensal bacteria has provided the scientific rationale for microbiome reconstitution as measure against the allergy epidemic [9]. However, the results from probiotic treatments have been conflicting [10–13]. The continuous confirmation of the hygiene hypothesis [14] and failure in current intervention methods suggest a need to research in new directions [15,16].

Recent studies on immigrants indicated that environmental changes later in life alone could lead to allergic diseases for adults who are equipped with immune systems developed in a relatively traditional lifestyle [17–19]. In several studies of Italian populations, immigrants who visited doctors with complaints of allergies had little family history of atopy [18,19]. Only 16% had a clinical history of allergies before migration. The time that elapsed between migration and onset of symptoms was 5.3 ± 3.1 years,

with a minimum of 0.5 and a maximum of 7 years. These immigrants were from Asia, Africa, South America, and Eastern Europe. A study of US immigrant children showed that children born outside the United States have a lower prevalence in allergic diseases that increases after residing in the United States for a decade [20].

Hypothesis

The combination of these research results prompted me to propose a specific hygiene hypothesis (SHH) and a capacity competition theory (CCT) to explain the rising of hay fever. SHH posits that continuous improvement in oral hygiene practices in modern society is the major cause of the increase in the prevalence of hay fever and perhaps some other allergic diseases as well (Fig. 1A). CCT is proposed to explain how reduction of oral infection, one of the results of modern oral hygiene, leads to development of allergy (Fig. 1B). CCT assumes that bacterial antigens under chronic oral infections have a much higher concentration than pollens do in oral-rhino cavities. The dominant bacterial antigens overwhelm the acquired immune system residing in lymph nodes at the back oral-rhino opening or nearby places, which limits the chance of immune system to access allergens and to produce B cell clones with efficient antibodies against allergens. After removing oral infections with persistent modern oral hygiene practices, reduced bacterial antigen concentration leaves extra antibody-generating capacity to allergens, with relative concentration becoming higher. The probability to produce B cell clones with highly efficient antibodies against allergens increases. The elevated innate immune system under infectious conditions can also clean allergens faster than that under conditions without infections, which further

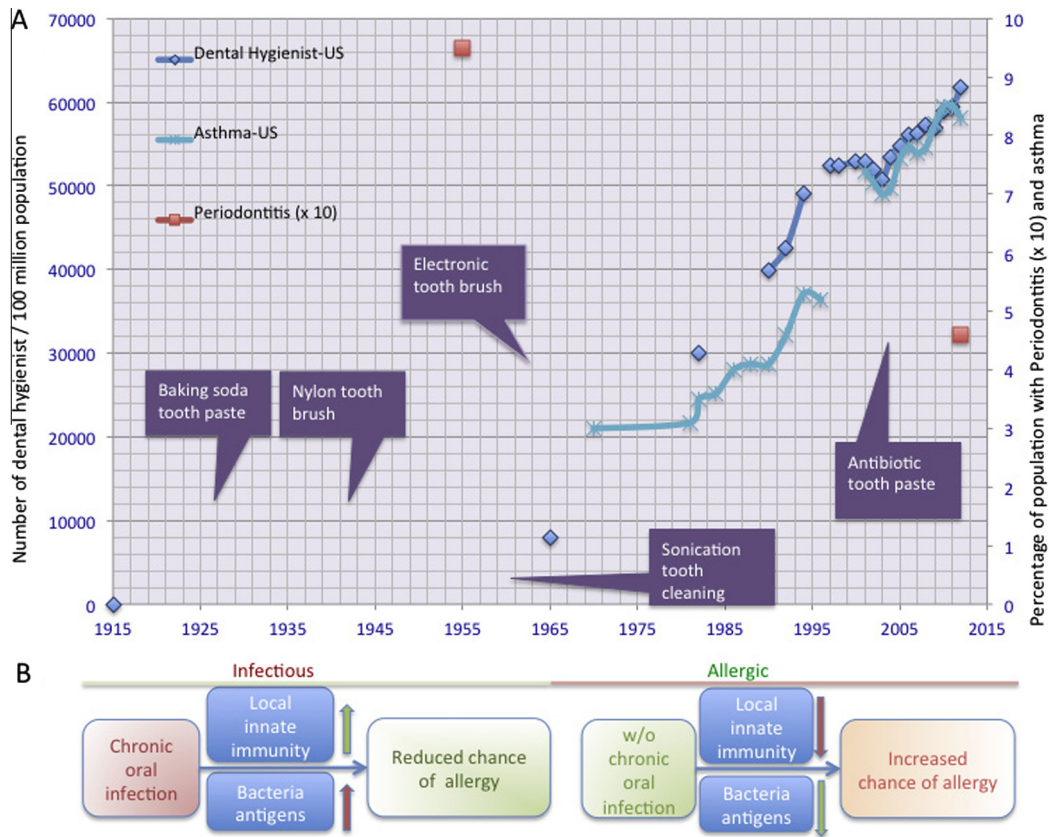


Fig. 1. The specific hygiene hypothesis and capacity competition theory. (A) Correlation between the number of dental hygienists, asthma prevalence in the US ($\text{cor} = 0.96$, $p \ll 0.01$), and reduction in prevalence of periodontitis suggest a relationship between oral hygiene and allergy. (B) The capacity competition theory (see text).

reduces the competitive edge of allergens (Fig. 1B). For the same reason, the stimulated innate immunity can likely protect against acute infections [21]. CCT indicates that the competing bacterial antigens do not have to be from a/multiple specific species.

SHH is different from GHH in the following aspects: 1) it specifies modern oral hygiene practices as the cause for the high rise of hay fever through the reduction of oral infection (Fig. 1B). 2) This hypothesis suggests actionable practices to prevent allergy if proved. 3) CCT indicates the importance of the local immune system in allergy development, though some bacteria might systematically relieve allergic reaction [22]. 4) CCT indicates lasting chronic infections have more protection against allergy than acute infections.

Besides the observed negative association between periodontitis, or periodontal microflora, and respiratory allergic diseases, studies on the dose-response effects of allergens also support the capacity competition theory [23–26]. A study found there is a sigmoid dose-response curve for subsequent reactivity [27]. Another study shows that local pollen counts are positively related to the prevalence of hay fever in children of different states in the United States [23].

The first evidence for the SHH is a high correlation between oral hygiene and the prevalence of allergic diseases (Fig. 1 and Supplementary Table 1). The oral hygiene level in a population can be measured in several ways, such as the consumption of oral hygiene products, frequency of dental visits, percentage of the population with dental insurance, and/or dental health condition. I choose to use the historical number of dental hygienists as the indicator of oral hygiene levels in US as data is readily available at the US Bureau of Labor Statistics. The profession of dental hygienist is a relatively new one, appearing first in 1915 with the main purpose

of cleaning and polishing teeth to prevent dental diseases. They also give visitors advice on their daily oral hygiene practices. The employment in this occupation has been steadily increasing since its creation. There were about 15 thousand dental hygienists in the US in 1965, before the increase in allergic diseases, and now there is a total of more than 193 thousand dental hygienists in US. The asthma prevalence data was collected from the Center for Disease Control. Linear regression shows that the two data sets are closely associated with each other ($r = 0.96$, $p \ll 0.01$, Fig. 1A and Supplementary Table 1).

The traditional oral hygiene status is infectious. The oral cavity is the entry to the digestive tract, which is where the battle between foreign bio-agents and our immune system begins. Without intentional help from the human host, the battle between foreign agents and the immune system is continuously visible. Oral infections are common in the population without modern hygiene practices. The study of an indigenous Native American population in Central America indicated a high prevalence of pocketing, and 90% of adults (≥ 35 years) had at least one site with clinical attachment levels (CAL) ≥ 6 mm [28]. A study based on the US population indicated that close to 80% of youth (13–15 years old) have gingivitis and more than 95 percent of the older population (≥ 35 years old) had periodontitis in the 1950s [29].

Oral hygiene practices began in ancient times, before recorded human history. Various excavations done throughout the world have recovered sticks, tree twigs, bird feathers, animal bones and porcupine quills that were chewed on to clean teeth [30,31]. However, only recently are we gradually winning the war against oral microbiota, with better and better toothbrushes, toothpaste, mouthwash, and floss. Early toothbrushes made of animal hair were neither effective, due to contamination of bacteria, nor

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