

Let them eat dirt...

..but don't forget the hygiene

THE 'HYGIENE Hypothesis was first postulated in 1989 by Strachan¹ who reported an inverse relationship between family size and development of atopic disorders. From this, he hypothesised that a lower incidence of infection in early childhood, transmitted by unhygienic contact with older siblings, or acquired pre-natally, could be a cause of the rapid rise in the atopic disorders over the last thirty to forty years.

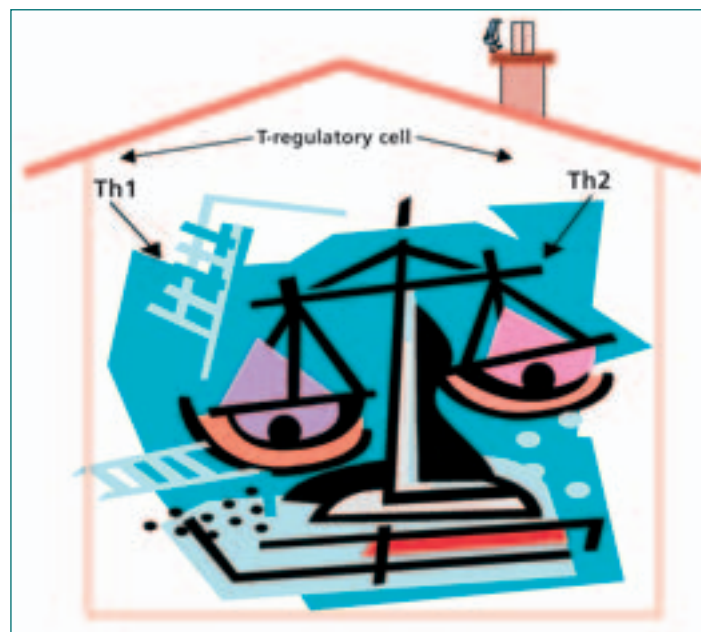
A further aspect of Strachan's hypothesis was his proposition that the reason why this exposure no longer occurs is, not only because of the trend towards smaller families, but also "improved household amenities and higher standards of personal cleanliness". The decision to name it the "hygiene" hypothesis made it memorable but is possibly misleading. With the significant attention from the media, the popular notion has arisen, that we have become "too clean for our own good".

The publicity given to this concept has aroused concern amongst infectious disease (ID) specialists who fear that publicising the idea of being "too clean" could have a detrimental impact on the public's perception of ID risks, and the importance of controlling them. In response to these concerns the International Scientific Forum on Home Hygiene (IFH) (www.ifh-homehygiene.org) commissioned a review of the hypothesis and its implications for hygiene, particularly in the domestic setting. The review addressed two distinct aspects

of the hypothesis:

- the evidence for a causal link between reduced microbial exposure and the recent rises in atopic disease
- whether cleaning and hygiene, as opposed to other influences on microbial exposure, could be a significant factor

This review summarises the main findings of the report².



The link between atopy, and microbial exposure and infection

Although many of the studies cited in support of the hygiene hypothesis are based on proxy measures of microbial exposure, some provide striking evidence supporting a causal link between atopy and microbial exposure. A consistent finding is the inverse relationship between atopy, family size and, to a lesser extent, birth order. There is also an apparent protective effect for children brought up on a

farm. In addition there are numerous contradictory studies, and overall the evidence remains inconclusive.

Some proponents suggest that the infection exposure necessary for the critical immune priming should be sufficient to cause clinical disease. ID surveillance trends do not support a temporal relationship with the rapid rise

or those which have re-surfaced (e.g. tuberculosis).

Introduction of measures to reduce ID, such as improved housing, sanitation and clean water, correlate with the decline in enteric diseases during the early 20th century, rather than the later rise in atopy. Reduced consumption of food-borne pathogens is also an unlikely candidate since the incidence of food poisoning rose during the critical period of the rise in atopy.

Intuitively, the idea that exposure to invasive infection, with all its attendant risks, might be needed to protect against atopy seems inefficient in evolutionary terms. A more plausible proposition is that exposure to milder endemic infections is the key. As far as morbidity is concerned, however, there is no evidence of a decline across the broad range of gastro-intestinal, respiratory and other common infections.

Additionally, although the findings of a recent study in Denmark³ confirm that larger family sizes, early childcare, pet keeping and farm living correlate with decreased risk of atopic dermatitis in children before 18 months, the data suggests that development of ID in early life is associated with increased, rather than reduced, risk of atopic dermatitis.

An alternative possibility is that 'background' exposure to "subclinical" doses of pathogens, or to commensal or environmental microbes, or perhaps to endotoxins, is the key. In a recent paper Rook⁴ proposes that immune dysregulation associated with increased risk of atopy is a ▣

in atopy in the 1970s - 1980s. The decline in serious infections such as cholera, typhoid and tuberculosis occurred too early to be associated with the late 20th century rise in atopic disease. The decline in measles in the UK dates from the introduction of the national vaccination programme in 1988. Similarly, the decline in hepatitis A virus since 1994, following the introduction of an effective vaccine, postdates the rise in atopy. Whilst "old" infections have declined, this has been offset by the emergence of new infections,

consequence of decreased exposure to microbes that are “old friends”, because of their continuous presence throughout mammalian evolution. He proposes that organisms such as saprophytic mycobacteria, helminths and lactobacilli are recognised by the immune system as harmless, and as adjuvants for immune regulation. The protective effect of farm living is consistent with the possibility that ‘background exposure’ from our outdoor environment is a factor.

Despite some good evidence supporting a link between microbial exposure and atopy, clear evidence is still lacking as to the nature of the critical changes in microbial contact that might have occurred, whether it is the general level of exposure which is important, or exposure to specific microbes, whether exposure is only important at certain times of life, whether the route of exposure is important etc.

The link between atopy, microbial exposure and hygiene practice in the home

The second question is whether the changes in microbial exposure, which may be causing immune dysregulation, are the result of modern trends in hygiene and personal cleanliness.

Evidence of a link with domestic hygiene is weak. Data published since the 1980s suggest that modern homes, whatever their visual appearance, still abound with a rich mixture of bacteria, viruses, fungi and moulds, as well as dust mites and other insects, and that opportunities for exposure are likely to have increased rather than decreased, since a rising proportion of time is spent indoors.

Microbes are continuously brought into the home via humans, animals, food etc.

Transmission of these microbes via hands, surfaces and cloths, during normal daily activities, provide ample opportunities for exposure to foodborne pathogens or pathogens from infected people or pets, as well as exposure to commensals and environmental microbes. There is no evidence that increased consumption of cleaning products is associated with more time spent on home cleaning; the per capita consumption for individual European countries show no correlation with levels of atopy. In reality, routine daily or weekly cleaning has little effect in reducing microbial exposure, even where they involve use of a disinfectant. Re-colonisation of surfaces rapidly occurs and many species are adapted to survival for long periods, particularly on damp surfaces, but also on apparently dry surfaces. Contrary to perception, cleaning can actually increase the distribution of microbes in the home. Whilst “hygiene” practice (i.e the specific actions we take to prevent transmission of disease) has been shown to be associated with reduced infection rates, observational studies indicate that consumer adherence to basic hygiene rules remain poor, suggesting that we are regularly exposed to pathogenic as well as commensal and environmental microbes.

The suggestion that trends towards more frequent showering and bathing show a temporal correlation with the rise in atopy is superficially consistent with the results of the ALSPAC Study⁵, but requires further investigation. The study showed a relationship between “hygiene scores” and atopy in young children, but focussed on “routine cleansing” rather than “targeted hygiene” i.e “parents were scored according to how

often in a day they wiped the child’s face and hands, whether hands were wiped before meals and how often the child was given a bath or shower”.

From the evidence linking atopy to declining family size, it can be argued that, regardless of hygiene behaviour, a decrease in the number of people in the home inevitably decreases opportunities for person-to-person transfer of human commensals, or case-to-case spread of infections via direct or indirect contact or airborne transmission. However, if exposure to childhood infections or commensals is

the non-pathogenic microbial flora of water or foods consequent on changing technologies of water purification and food production etc, but since food and water is only routinely monitored for pathogen content there are no data to show what these trends might have been. Alternatively the changes may have been generated by the introduction of antibiotics. Although this fits well with the rise in atopy in temporal terms, the supporting evidence is inconsistent. The balance of evidence is also against vaccination as a causative factor. More important



important it should be found that the effects of declining family size are offset by increased opportunities for exposure from attendance at day nursery. Although there is some supporting data, other studies show no evidence of a protective effect.

Quite apart from hygiene, there are a number of other lifestyle, medical and public health trends which could equally well have caused incidental changes in microbial exposure, manifesting as increased risk of atopy. For example, changes will have occurred in

perhaps is the significant evidence supporting a range of ‘non-microbial’ factors, such as diet, obesity and lack of exercise which may be causative factors in the rise in atopy.

The implications for hygiene practice

On the basis of current evidence, relaxing hygiene standards seems neither justified, nor rational. On the contrary, current concerns about ID provides compelling reasons why we should not do this.

Although ID mortality is

declining in the developed world, trends in morbidity suggest changing patterns of ID rather than declining rates. This is partly associated with the continual emergence of new infections, such as *Campylobacter* and *Escherichia coli* O157, and re-emergence of old pathogens such as tuberculosis. Infectious intestinal diseases remain at unacceptably high levels, but could be greatly reduced through better standards of hygiene. Globalisation of food markets, increased travel and refugee movements mean that pathogens more readily and quickly reach areas where

same applies in most European countries. In addition, pathogens are increasingly implicated as co-factors in cancers and some degenerative diseases.

Developing a rational approach to home hygiene

Regardless of whether the hygiene hypothesis is correct, the popular interpretation that 'dirt is good for us'⁶ has considerably influenced attitudes, and caused loss of confidence among the public regarding home hygiene. One positive benefit however is a recognition by public health professionals of the need to

practice, the IFH has produced guidance documents on home hygiene^{7,8}. The key feature of the guidelines is that they are based on the concept of risk assessment and risk prevention⁹. The guidelines start from the premise that homes always contain harmful microbes (from people, pets, food, etc.) and that ID prevention is about targeting measures in the places and at the times that matter, in order to limit risks of exposure. Hygienic cleanliness (reduction to a level that does not pose a significant threat) is required only where infection risk is significant, e.g. after contact with excreta, during food preparation etc. Whatever the reality regarding the hygiene hypothesis, "targeted hygiene" makes sense because it seeks to maximise protection against ID, whilst retaining any beneficial effects which microbes may have on our human and natural environment.

Although this review concludes that the relationship

of the hypothesis to hygiene practice is not proven, it lends strong support to initiatives seeking to improve hygiene practice. It would however be helpful if the hypothesis were renamed, e.g. as the 'microbial exposure' hypothesis. Avoiding the term "hygiene" would help focus attention on determining the true impact of microbes on atopic diseases, while minimising risks of discouraging good hygiene practice.

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there is little innate resistance. There is now evidence that hygiene plays a role in reducing the spread of cold and flu viruses. Of particular concern is the rising proportion of the population who are more vulnerable to infection. This includes the elderly, the very young, people with chronic or degenerative illness and immunocompromised patients discharged from hospital, all of whom are increasingly cared for at home. Currently, about one person in six in the UK belongs to an 'at risk' group, and it is likely that the

provide clearer guidance. One of the concepts which we need to clarify in the mind of the consumer is the difference between "dirt" and "germs", and between "cleanliness" and "hygiene". Without knowing the nature of the microbial exposure which may be critical for immune priming, it is difficult to reformulate hygiene policy, in favour of improving immune function without compromising protection against ID, but some progress is being made.

As a part of its work to promote better understanding of hygiene and better hygiene

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