Are We Too Clean For Our Own Good?  
Dr. Sally F. Bloomfield, London School of Hygiene and Tropical Medicine  
A Webber Training Teleclass

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Aims and Objectives of teleclass

- Understand the hygiene hypothesis: how our understanding of the link between microbial exposure, and allergies and other chronic inflammatory disorders is now developing
- Consider the factors which have contributed to loss of the microbial exposure required for immune regulation
- Consider what measures could be used to reverse trends in allergies/CIDs.
- Consider the implications of new understanding for hygiene practice, life styles and public health

How has our understanding of the hygiene hypothesis developed?

Although role of microbial exposure in immune regulation now widely accepted – 2 major developments:

- Concept applies to a range of chronic inflammatory diseases (CIDs):
  - Allergies: asthma, hayfever, food allergies
  - Type 1 diabetes (T1D), multiple sclerosis (MS)
  - Inflammatory bowel disease (IBD)
  - Some types of depression and cancers.

The hygiene hypothesis – what does it mean?

- Much debate about extent to which children should be protected from ID – could this be linked to rapid rise in allergic diseases since 1960/70s
- 1989 Strachan proposed - rise in allergic diseases related to lower incidence of infection in early childhood
- Based on research showing:
  - Larger family size protects against hay fever
  - Living on a farm protects against asthma
- Named “Hygiene hypothesis”
- From this - notion "we have become too clean for our own good" has arisen.

The hygiene hypothesis and its implications for home hygiene, lifestyle and public health

- 2012 IFH report
- Summary of findings/conclusions
- IFH website - www.ifh-homehygiene.org
- Summary also in hard copy
- Thanks to Prof Graham Rook and Dr Stanwell-Smith

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The Old Friends Hypothesis

Proposed by Rook in 2003:
• microbial exposures not IDs (colds, flu, measles, norovirus etc) evolved over the last 10,000 years – the “crowd infections”
• But – microbes we co-evolved with in Paleolithic times – human immune system was developing.
• Evolved dependency on microbial exposure – our immune systems have become so dependent on these exposures that they cannot function properly without them
• Rook hypothesizes: immune system evolved to require input from at least three sources that we collectively term the Old Friends
• Note: also sometimes called “microbiome depletion hypothesis”

“Old Friends” include:

<table>
<thead>
<tr>
<th>Commensal microbiota: normal microbiota of skin, gut, airway, urogenital, etc</th>
<th>Transmitted by mothers and other family members</th>
<th>Diminished diversity and exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environmental microbiota (animals, soil, air, plants)</td>
<td>Spp. which inhabit our indoor and outdoor environments</td>
<td>Diminished diversity and exposure</td>
</tr>
<tr>
<td>Old infections – can persist in hunter-gatherer groups: Helminths Salmonella, HAV, H. Pylori etc</td>
<td>establish chronic infections - have to be tolerated, attempts to eliminate cause tissue damage</td>
<td>mostly lost</td>
</tr>
</tbody>
</table>

“Crowd infections”:

- “recently” evolved childhood infections: measles etc
- All or immune, cannot persist in hunter-gatherer groups
- Increased – especially in inner cities

How does it work – asthma and allergies?

• Immune system reacts against dust, pollen etc
• Once threat eliminated, reaction shuts off
• Without immune regulation, system may overreact, which is underlying cause of allergies/ CIDs.
• Hygiene hypothesis proposes that microbial exposure is key part of the maturation of regulatory system

How does it work – autoimmune disease?

• Immune system recognises “self”
• Does not attack own tissues
• Without immune regulation, system may overreact, attacking our own tissues → autoimmune diseases
• Hygiene hypothesis proposes that microbial exposure is key part of the maturation of regulatory system

Microbial diversity hypothesis

Exposure needs not confined to single species - can be met by one or more of diverse range - any species missing, role met by others

Diversity and turnover of bacterial species is a requirement, rather than stable colonisation with one species.

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Do exposures need to be maintained during childhood and adult life?
- Most important – during pregnancy, first days or months - but needs to be maintained for significant period e.g. Breastfeeding for 6 m
- Some evidence on-going exposure may be important
  Oral treatment of adults with IBD or MS with helminth eggs → significant improvement of symptoms

Why has this happened - and why now?
- Allergies/CIDs existed prior to 1800s - largely diseases of last 200 years
- Hay fever so rare in the late C19th - doctors struggled to find cases to study - now estimated 10 million in UK.
- Accumulated data
  - Increasing levels from the late 19th century
  - Rapid rise from the 1970s

What has changed in past 2 centuries to deprive us of requisite microbial exposure?

Obvious answer - sanitary/ hygiene revolution.
- improved water quality, sanitation,
  - occurred gradually from 1800s but, (e.g., widespread coverage (toilets, chlorinated drinking water etc) did not occur until late 19th into 20th
  - environmental clean-up - reduced exposure to human waste and animal excreta in city streets.

Altered diet/foods (different or less microbial content)

If the OF hypothesis is correct
- Temporal correlation suggests that these factors are involved
- Seems likely that not one – but all of these factors are involved
- but not for obvious reason i.e need for pathogen exposure
- Vital protection from ID, but inadvertently reduced/ altered exposure to “microbial old friends”

Could antibiotics be involved?
- Antibiotic usage - good temporal fit
  - Increasing antibiotics since 1950s
  - Steep rise in allergies from 1970s

- Growing evidence from epidemiological studies that antibiotics may be a factor – particularly excessive AB use during pregnancy/neonatal period
  - Evidence for asthma, cow’s milk allergy, IBD, eczema

- antibiotics may alter our interaction with microbes - reduced diversity of gut microbiota
- Need to monitor closely

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What about vaccines?

• Immunisation against tetanus and diphtheria introduced during 1930s/40s, followed by vaccines against several childhood infections.

But

• Epidemiological studies provide no consistent support for detrimental effect on atopy rates.

Is microbial exposure the only factor?

• Increased risk of allergies/CIDs also depends on other factors:
  – diet (vitamin D deficiency), pollution, less physical activity, obesity,
  – socio-economic factors and stress,
• Genetic predisposition - key risk factor.

Microbial “Old Friends”, immunoregulation and socio-economic status GAW Rook, CL Raison CA.  
Lowy  

• Rook: “hygiene hypothesis is now a misleading misnomer – it’s no longer a hypothesis and it’s not about “hygiene”.
• Review sets out framework showing how lifestyle & medical changes over the past 2 centuries have worked together to inadvertently deprive us of key microbial exposures, and trigger epidemic of allergies and other CIDs.
• “To tackle this problem, we have to stop talking about it as a consequence of our “modern obsession with cleanliness”.

Progressive loss of exposure to OFs

<table>
<thead>
<tr>
<th>Sanitation, water, waste disposal etc</th>
<th>Loss of “old infections”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caesarean delivery, antibiotics, diet</td>
<td>Disturbed human microbiota</td>
</tr>
<tr>
<td>Less contact with animals and green spaces</td>
<td>Reduced microbial inputs from the “natural” environment</td>
</tr>
<tr>
<td>Urbanisation sustains high exposure to crowd infections, GI, RT, skin etc infections circulating in community continue to exert heavy toll</td>
<td></td>
</tr>
</tbody>
</table>

From Rock, Raison & Lowry

Are we too clean for our own good?

• Role of home and personal hygiene small relative to other factors.
  – Clean-looking homes full of bacteria, viruses, fungi, etc.
  – Routine weekly cleaning - no sustained effect on microbe levels
• Cannot create “sterile” home - microbes constantly replaced via dust, air, body flora, pets, contaminated foods.

Key point may be:
• Microbial content of homes now DIFFERENT - but not because of “increased” cleanliness
  – e.g modern urban homes – interact c different environment cf rural homes prior to 1800s
  – helminths now relatively rare - up to 1950s 50% children infested with pinworm

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What about personal hygiene?

- Strachan suggested that “higher standards of personal cleanliness” could be an underlying cause
- Temporal correlation i.e increased bathing/showering, shampooing/bathing baby since 1950s
- Bathing and showering remove microbes from skin but rapidly replaced and no evidence that it includes OFs
- No evidence linking frequency of washing, showering or bathing to increased allergies risk.
- Need to monitor?

How might we reverse the trends in allergies and other CIDs?

- Therapeutic approaches
- Using probiotic drinks or foods to reintroduce the key microbes to our bodies
- Progress requires better understanding which ‘old friends’ are truly friendly – and safe.

Parker and Ollerton. Evolutionary biology and anthropology suggest biome reconstitution as a necessary approach toward dealing with immune disorders. Evolution, Medicine, and Public Health [2013] pp. 89–103

Could lifestyle changes re-establish our exposure to OFs?:

- For example
  - encouraging natural childbirth,
  - encouraging sustained breast feeding,
  - physical interaction between siblings,
  - more sport and other outdoor activities.
- Important to be cautious.
  - Reconnecting with environment, getting dirty, could contribute
  - BUT - need clearer understanding before these approaches could be strongly advocated.

Where have we got to?

- Reversing trends in CIDs
  - Rook: “The work is progressing very fast, but it has a long way to go”
- Controlling infectious diseases
  - Good news! - allergies/CIDs not the price we have to pay for protection against IDs

Why is hygiene in home and everyday life so important?

- Infectious disease circulating in the community - heavy burden on health and healthcare systems
- Much preventable by good hygiene in homes and everyday lives
- Hygiene related disease includes:
  - Gastrointestinal (food and non-food e.g norovirus)
    - UK - 17 million cases of IID pa, 1 in 4 people [Tam et al 2011]
    - UK norovirus – 3 million - mostly non-foodborne
  - Emerging infections – new agents/strains
    - SARS, influenza “pandemic” strains
    - E.coli O104
- Increasing “at risk” groups needing special care
  - Up to 1 in 5 people in the European community
  - Including - otherwise healthy - elderly, very young, pregnant
  - underlining disease: HIV/AIDS
- Increasing healthcare at home /in community
  - shorter hospital stays
  - home-based treatments: chemotherapy, dialysis etc
  - Much of healthcare is by family members
  - food hygiene, respiratory hygiene are also important

ID risk in the community is increasing

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Antibiotic resistance

Tackling antibiotic resistance is a global priority:
- Involves home and community as well as hospitals
- Hygiene now seen as a central strategy to reducing AR
  - Prevention through hygiene:
    - reduces the need for antibiotic prescribing
    - Reduces “silent” spread of AR strains such as MRSA, NDM-1
  - As spread of nasal/gut etc carriage in healthy population increases - risk of hospital and community infections increases.

Can we have it both ways?

- If prevention of ID in children through good hygiene remains a cornerstone of public health
- But
  - if the ‘right kind’ of microbial exposure needs to be encouraged,
  - How do we address both issues at the same time?
  - How do we persuade people to develop lifestyles which reconnect with the “natural” environment whilst also protecting themselves and their children from ID?

We need to unravel the confusion

“we have become too clean for our own good”.

- What do we really mean? – are we/they saying:
  - We need to encourage children to get dirty?
  - we need to relax hygiene standards?
  - children who have more infections are less likely to develop allergies

Daily Mail

‘Inevitable’ flu pandemic will kill 75,000 Britons and 50 million worldwide, warn Lords

Is your supermarket chicken poisoning you?

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We have to change attitudes and understanding?

- Need to distinguish cleanliness (absence of dirt, social acceptability, freshness) from infection prevention practices.
- ID avoidance not about how clean our homes look/how often we shower, etc.
- Its what we do at times when it matters to stop spread of germs:
  - ALWAYS washing hands
  - after toilet & handling raw foods
  - before handling ready to eat foods.
  - After changing babies nappy
- Rigorous food hygiene in the kitchen
- Good respiratory hygiene (catch it, bin it, kill it)
- Following the hygiene rules when caring for pets.

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Example of “getting more dirty” to protect children from allergies?

- 3x less likely to suffer from eczema at 1.5 years of age,
- No more upper respiratory infections were seen in the children whose parents sucked on their dummies.

Targeted hygiene and sustainability

- Preventing infection intrinsically more sustainable approach than treatment.
- Sustainability of hygiene practice must be considered
- Targeted/multibarrier hygiene c focussed interventions provides a framework for building sustainability into hygiene
- Because:
  - Maximises protection from pathogen exposure risks
  - minimises environmental impact by discouraging overuse of cleaning products
  - minimises AR risks through low level microbicide exposure.
  - Targeted hygiene can help to restore OF exposure without restoring pathogen exposure

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Conclusions

- Allergies are serious public health problem
- Other CIDs – IBD, MS, T1D etc
- Infectious diseases preventable by good hygiene

"Using home and personal cleanliness as a scapegoat for problem that has a much more complicated set of causes not only unjustified, but ill-advised - diverting effort from finding true causes and workable solutions which address all of these health issues"
- In the future we are going to have to view our microbial world very differently?

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