Understanding the epidemic of asthma and allergy

Miegunyah Lecture 2012
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But what are those environmental factors?
- Contrary to expectations draconian allergen reduction strategies failed to impact on either the origins of asthma in high risk children or established asthma!
- By reducing dust mite exposure, are we reducing other critical elements of exposure in the environment?

“We suggest that exposure to higher allergen levels has increased airway abnormalities in atopic children or that mechanisms that protected airways of earlier generations of children have been altered by new environmental factors”.

Risk of allergy associated with microbial components in house dust in Finland

The greater the microbial load The less the risk of allergy

Changes in prevalence of diagnosed asthma (A) and asthma symptoms (B) over time among children and young adults.

The last 10 years has witnessed a dramatic increase in asthma and allergies in countries that are rapidly developing such as Africa and China

The Karelia Allergy Study: younger generations are more allergic in Finland but not in Russia

Evolution of microbial exposures and disease

Microbes in environment

Paleolithic (from 2.6 million - 10,000 yrs ago): Hunter gatherer small groups by lakes and rivers; scavenging

1ST EPIDEMIOLOGICAL TRANSITION
Neolithic (10,000 - 3,000 yrs BC): Larger social groups, animal husbandry, prolonged animal contact, domesticated cats & dogs + rodent pests, increased oro-faecal transmission.
Bronze age (2-3,000 yrs BC): Larger communities = Influenza, mumps, small-pox, measles, plagues (including endemic infections).
Iron age to pre-industrial age (about 1500 BC to 1800) 97% still living in rural environment e.g. farms, animal & mud contact, untreated water
Plagues and epidemics but little change in everyday exposure since Paleolithic period.
2nd EPIDEMIOLOGICAL TRANSITION
Modern age (from early 19th century)

Change only in 10 years (1990-2000)
Landsat, satellite photos: Chengdu, Capital of Sichuan Province, China, 11 million inhabitants
Ji Jinping: the ‘big personality’ taking charge in China

Lifestyle factors associated with increased allergy and asthma
- Urban vs rural living (West vs East) ↑
- Being brought up on a livestock farm ↓
- Antibiotics in pregnancy and early life ↑
- Birth order and large family size ↓
- Caesarean section ↑
- Anthroposophist lifestyle ↓
- Communal day care ↓
- Oily fish intake ↓
- Paracetamol in pregnancy and infancy ↑
- Maternal tobacco smoking ↑
- ? Air pollution and environmental chemical exposure ↑
- Parasite infection ↑

“The Hygiene Hypothesis”

Bavarian women milking cows and their offspring exposed to a unique inhaled and food environment

The diversity of microbial exposure is inversely related to asthma
Inhibitory influence of living on a livestock farm over the development of allergy


Louis Pasteur: the discovery of antibiotics

After serving briefly as professor of physics at Dijon Lycée in 1848, he became professor of chemistry at the University of Strasbourg, where he met and courted Marie Laurent, daughter of the university’s rector, in 1849. They were married on May 29, 1849, and together had five children, only two of whom survived to adulthood; the other three died of typhoid. These personal tragedies inspired Pasteur to try to find cures for diseases such as typhoid.

The 16S Ribonucleic acid (rRNA) gene is used for phylogenetic studies as it is highly conserved between different species of bacteria

Graphical representation of the 454 pyrosequencing technology


Schematic cross section of human skin: Microorganisms (bacteria, viruses, fungi) and mites cover the skin and live deep in the hair and glands

Bacterial distribution changes dramatically in airways disease such as asthma

Similar microbiome in young children with severe asthma

Adults
Children

Farm living: effects on childhood asthma and allergy

Contact with multiple farm animal species
Consumption of farm milk
Risk of asthma and hay fever

Urban environment reduces exposure to micro-organisms through the gut, skin and respiratory mucosa, and dendritic cells provide less challenge to immunoreactive T-cells

The microbiome is influenced by (and may determine) factors affecting asthma
Diet
Host genetics
Treatment
Environment
Immunity & previous infections

HEALTHY
Microbiome diversity
Few pathogens
Normal levels & diversity of commensals

ASTHMATIC
Increased incidence of pathogens
Decreased levels and diversity of commensals

Conclusions
1. Asthma and allergy are increasing worldwide as a consequence of urbanisation.
2. Environmental factors associated with lifestyle are the most likely drivers of such trends.
3. Alterations in the extent of stimulation of our innate immune response is the most likely mechanism for the increase in asthma (and other chronic inflammatory disorders).
4. Reduced diversity and intensity of microbial exposure, especially bacterial products, seems to be the prime culprit.
5. Increasing the level of protective immunity of the lung by altering the microbiome and/or raising the capacity to neutralise viral infection is more likely to be the most productive way of achieving protection against acute and chronic lung disease.
High diversity of microorganisms affects directly to immune system

- Saprophytes: Fungi, Parasites, Protozoas, Mites
- Continuous exposure via gut, respiratory mucosa and skin
- Strong and diverse antigen recognizing receptor and Treg network
- Tolerance: danger vs. non-danger
- Reduced risk of allergy and many other chronic immunological disorders

Biodiversity hypothesis – evolved from hygiene hypothesis and microbial deprivation hypothesis

Haathela T & von Hertzen L 2011

Species dying as fast as ever as 2010 conservation target passes

The Times April 30th 2010

- And, perhaps not surprisingly, the HMP discovered that microbial distributions in the human body are not so different from those in ocean ecosystems.
- There’s good reason to believe that destruction of species and the simplification of ecosystems that seem to be overtaking us, in addition to being an environmental, food, and social justice issue, is also a health issue.
  - Animal populations have fallen by 31 per cent since 1970, living corals by 38 per cent and mangroves and sea grasses by 19 per cent. The annual rates of loss have shown no improvement since 2002, according to the study of more than 40 international monitoring systems.
  - The main causes of species loss were all linked to human activities, including habitat destruction, hunting, the introduction of alien predators, the spreading of disease and climate change.

Mikeangello (6 March 1475 – 18 February 1564)
The creation of Adam
Sistine Chapel, Vatican City, Rome

- Microbes defy a simple notion of individuality.
- They are essential to our biology and they travel with us from birth to death.
- Yet, they also flow between us, and can be found in water, food and soil.
- The more we understand about the human microbiome the more we realise that everything is connected: humans