A simple guide to healthy living in a germy world

An **'Interactive Guide'** that explains our current understanding of the so-called hygiene hypothesis, how and why reduced interaction with our microbial world is linked to rising levels of allergies and other chronic inflammatory diseases.

The guide also looks at how we can develop hygiene habits which will protect us against infectious diseases whilst at the same time maintaining exposure to the microbes which are important for our health

This resource has been produced by the International Scientific Forum on Home Hygiene. The resource can be viewed online at: http://www.ifh-homehygiene.org/books/simple-guide-healthy-living-germy-world

Contents

What is this guide about?

This guide sets out to explain current understanding of the relationship between the rise in allergies and other inflammatory diseases, modern lifestyles, our interaction with our microbial world, and the need to protect against infectious diseases. It also examines the measures being developed to tackle these issues.

This guide explains the basic facts in easy to understand language

What is the fundamental question?

"How can we develop lifestyles, together with health policies, which reconnect us with the necessary microbial exposures, whilst also protecting against infectious diseases?"

Who is this guide for?

The guide is helpful for anyone wanting to know more about the ideas around 'being to clean for our own good' and the need to protect ourselves from infection

It may be particularly helpful to:

- community health workers (nurses, health visitors)
- general practitioners, pharmacists
- public health specialists
- health policy makers
- the professional and consumer media
- school teachers
- upper secondary school pupils

Introduction

The rise in Chronic Inflammatory Disease

In recent years there has been a massive rise in allergic and other Chronic Inflammatory Diseases.

The rise has been particularly great in the urban centres of Western society.

Why has this happened?

No single cause has been identified, but it is becoming clear that microbial exposure is a fundamental underlying factor.

Exposure, particularly in early life, to the diverse range of microbes that inhabit our natural, and our human and animal environments (usually referred to as the microbiome) is important for building and sustaining an immune system which is properly regulated.

Without regulation the system can overreact, or react inappropriately to allergens like pollen (causing allergies) or our own tissues (causing autoimmune diseases).

What about infectious diseases?

Since the microbial exposures we require are largely non harmful, we need to discover how we can reconnect with our microbial world without increasing our exposure to infection

What are Chronic Inflammatory Diseases?

Allergic diseases such as:

- Asthma
- Hay fever
- Eczema

and diseases such as

- Multiple Sclerosis (MS)
- Type 1 Diabetes (T1D)

Our Opinion

Whilst new knowledge suggests we need to reconnect with our microbial world, the idea that we should be less “hygienic” is wrong.

Relaxing standards of “hygiene” would not reverse the trend, it would only serve to increase the risks of infectious disease.

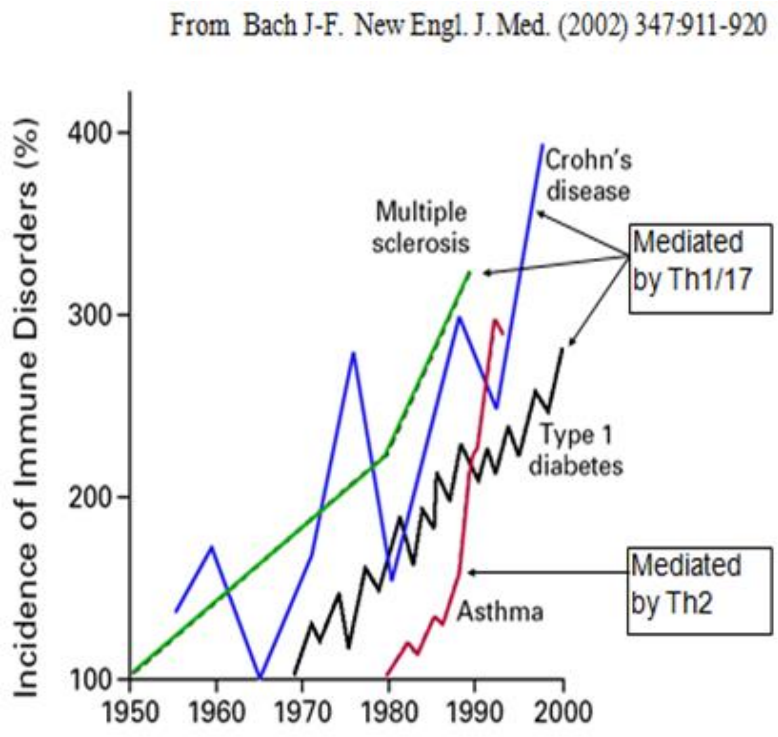
What do we know about the rise in inflammatory diseases?

In the last century, diseases caused by overreaction of the immune system have increased steadily, particularly from around the 1970's onwards. This has been especially the case for industrialised societies.

Allergies now affect as much as 50% of the industrialised human population.

Auto-immune diseases such as Type 1 diabetes and Multiple Sclerosis (where the immune system reacts against the body's own tissues) and other diseases involving inappropriate immune responses (e.g Crohn's Disease) are prevalent in at least 10% of industrialised populations.

Although many different factors play a role, it is becoming clear that exposure to microbes has a vital part to play



Did you know?

In the early 1900s, hayfever was so rare that doctors struggled to find cases to study.

It is estimated that 10 million people in the UK now suffer from hay fever

How does microbial exposure protect us from allergies and other chronic inflammatory diseases?

The link between microbial exposure and immune diseases

The concept of a link between reduced microbial exposure and the rise in allergic disease was first proposed by David Strachan in 1989 and was named the **Hygiene Hypothesis**.

Although the basic concept still appears to be correct, the proposal of a link to infectious disease and hygiene is now largely discounted. Refinements to the original hypothesis now offer a more plausible explanation

The hygiene hypothesis has been variously renamed as:

The Old Friends Mechanism,

Microbiome Depletion Hypothesis,

Microbial diversity hypothesis

The Old Friends (OF) Mechanism

The Old Friends mechanism was proposed by Graham Rook in 2003.

He proposed that the required microbial exposures are not infectious diseases (colds, flu, measles, norovirus etc) which evolved only over the last 10,000 years, but the microbes we co-evolved with in hunter gatherer times when the human immune system was developing.

Although these microbes are still there, through modern lifestyle changes we have lost our exposure to them

Evolved dependency on microbial exposure.

Our immune systems have become so dependent on these exposures that they cannot function properly without them

To learn more about the Old Friends mechanism go to page 40

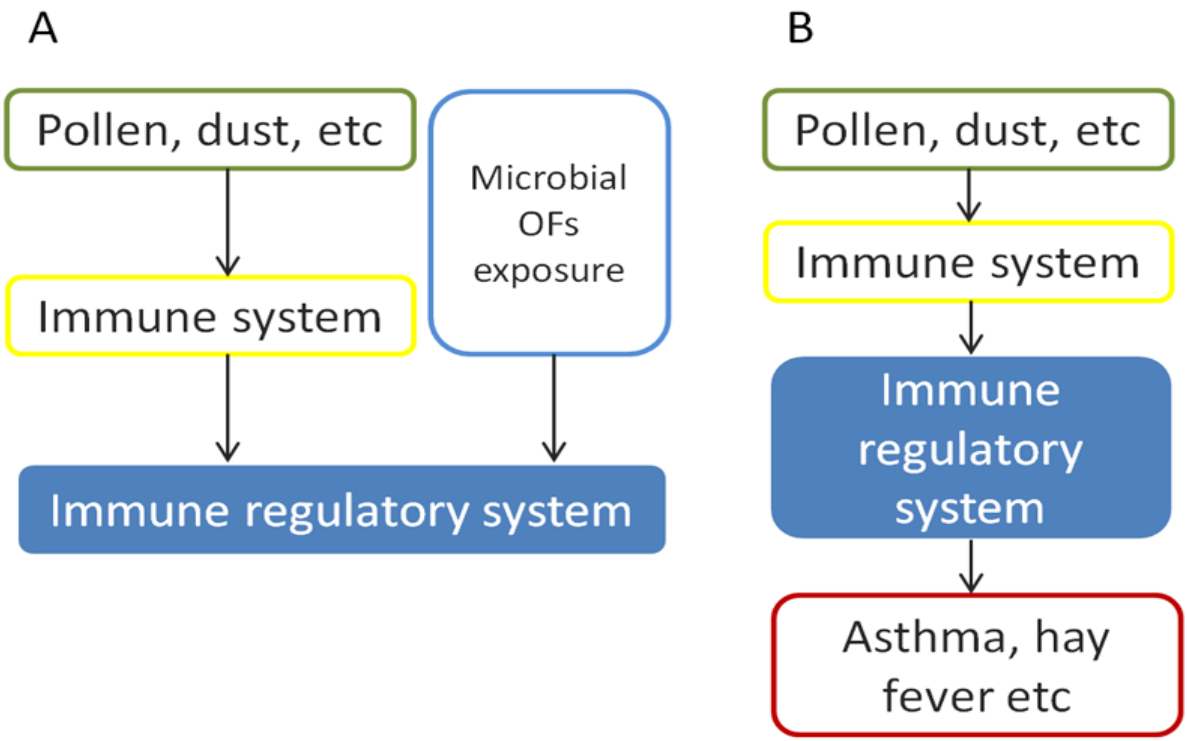
Who are our Old Friends?

Rook hypothesizes that the immune system has evolved to require input from at least three sources collectively called the Old Friends:

Commensal microbiota: diverse range of species found on normal skin, gut, airways, urogenitary tract, etc	Transmitted by mothers and other family members
Environmental microbiota: diverse range of species found on animals, soil, air, plants	Spp. which inhabit our indoor and outdoor environments
Old Infections: Helminths Salmonella, HAV, *H. Pylori etc*	Cause chronic infections - have to be tolerated, attempts to eliminate cause tissue-damage

How does it happen – asthma and allergies?

- **The immune system** reacts against dust, pollen etc.
- Once any possible threat is eliminated, the reaction shuts off (A)
- Without immune regulation, the immune system may overreact to the allergen, which is the underlying cause of allergies such as hay fever and asthma (B)
- The OF hypothesis proposes that microbial exposure (A) is a key to building and sustaining the immune regulatory system so that it reacts appropriately



further Reading

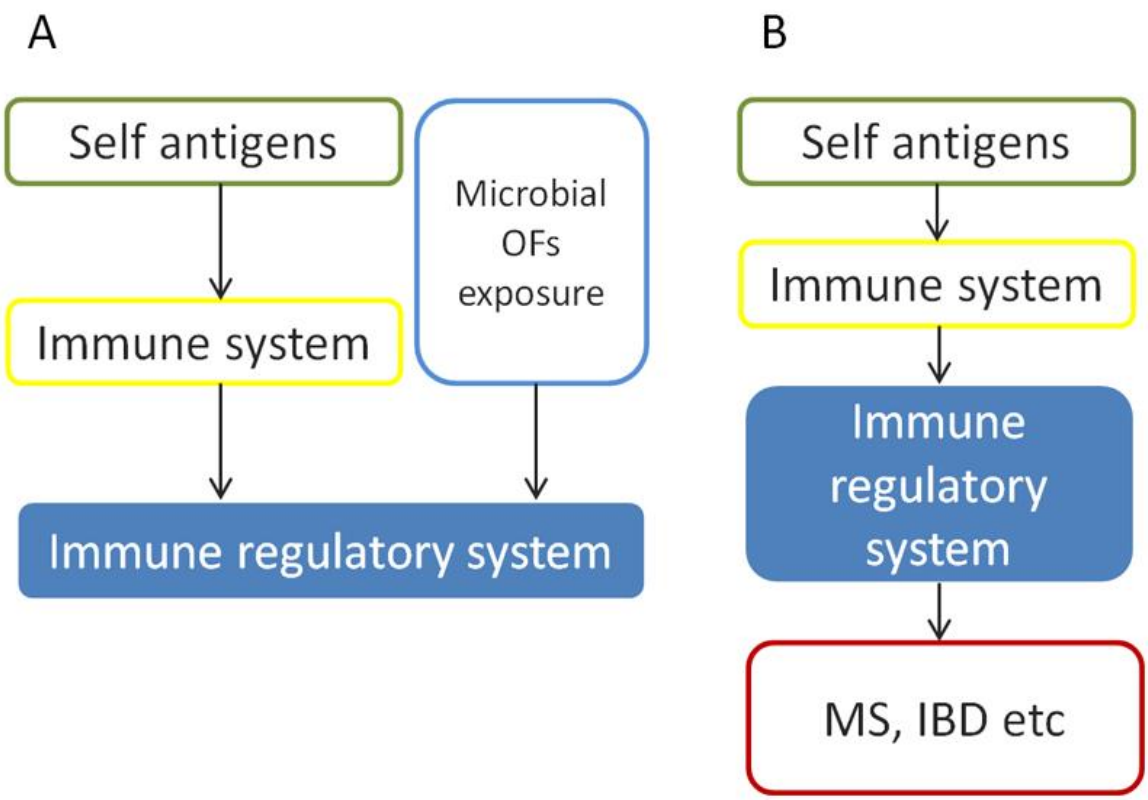
To read more about the immune system go to page 34

How does it happen – autoimmune diseases?

- **The Immune system** recognises “self” i.e. our own body cells. This is important to stop it attacking our own tissues

- Without immune regulation, the immune system may overreact and attack our own tissues (B)
- This can lead to development of autoimmune diseases such as multiple sclerosis and type 1 diabetes

- OF hypothesis proposes that microbial exposure (A) is key to building and sustaining the immune regulatory system to ensure that it does not attack our own body cells



further Reading

To learn more about the immune system go to page 34.

The importance of microbial diversity

It is thought that :

- Our microbial exposure needs are not confined to a single OF species
- Exposure to a diverse range of species is a requirement
- This may mean that our exposure needs can be met by one or more of a diverse range of microbes which make up the human and environmental microbiome
- If any species is missing, their role may be met by others

Swedish Study

A 2008 Swedish study showed that reduced diversity of faecal microbiota in infants at one week was associated with higher rates of eczema at 18 months

What is the route of microbial exposure?

Based on current evidence, the oral and respiratory routes seems the most likely candidate, which fits with the OF mechanism.

However, findings do not rule out other routes including inhalation, which is very effective in animal models, or even transdermal exposure.

Possibly all of these routes are involved.

Danish Study

A 2011 Danish study showed that increased risk of allergic disease was associated with less gut microbiota diversity in infancy

Does exposure need to be maintained during adult life?

Evidence suggests that **the most important time of exposure is during pregnancy, and during the first hours, days or months of life.**

Evidence suggests that exposure needs to be maintained for a significant period e.g. Breastfeeding for 6 m

There is some evidence that on-going exposure may be important

More research is needed. Most of our understanding comes from studies with infants

Oral Treatment

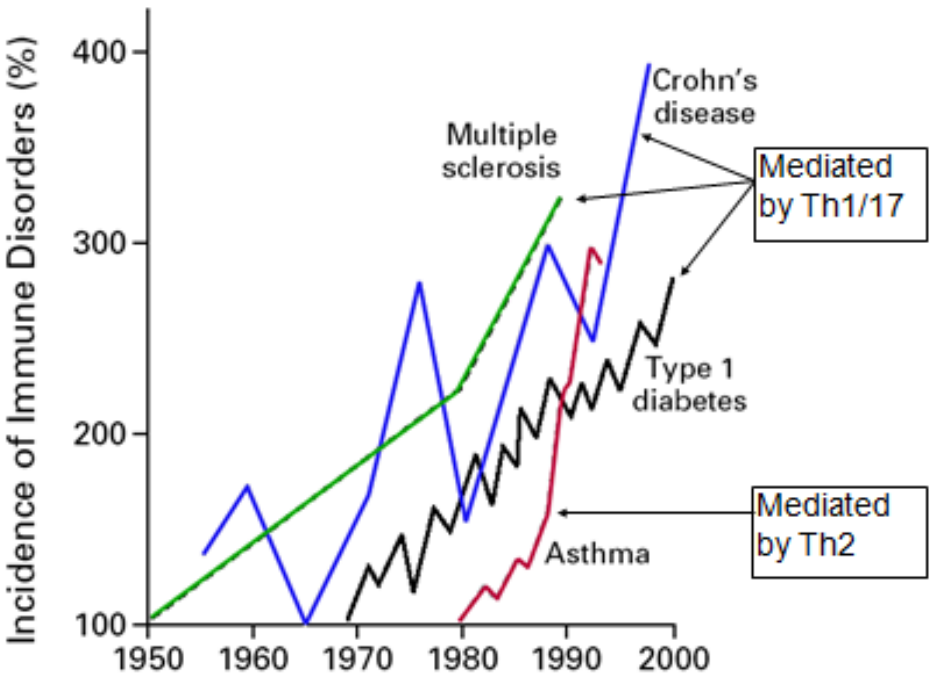
A 2007 study showed that, when adults with established Inflammatory Bowel Disease (IBD) or Multiple Sclerosis (MS) took part in trials involving oral treatment with helminth (worms) eggs, significant improvement of symptoms was seen.

It has been shown that naturally-occurring helminth infection can delay progression of established early MS

What lifestyle and other changes have caused the problem?

- Allergies/CIDs existed prior to 1800s – but are largely diseases of last 100 -200 years
- Accumulated data suggests
  - 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?
- It seems likely that not one – but all of the following factors are involved:

From Bach J-F. New Engl. J. Med. (2002) 347:911-920



The Sanitary Revolution

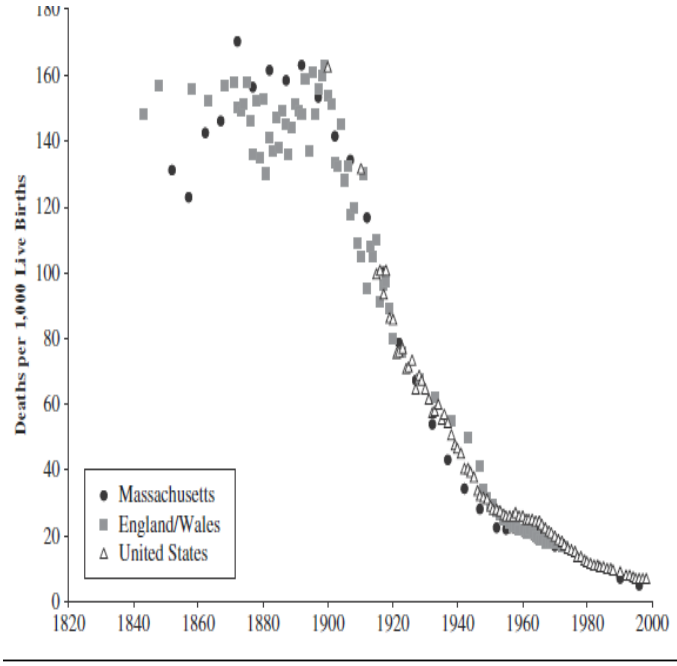
The obvious answer is the sanitary revolution of past 200 years.

Improved water quality and sanitation:

- occurred gradually from 1800s, but widespread coverage (toilets, treated water, etc) did not occur until late 19th into C20th
- environmental clean-up from 1850s - reduced exposure to human waste and animal excreta in city streets.

- Rapid decline in mortality 1900 - 1950 particularly young children.
- Decline in cholera, typhoid, TB, diphtheria, and common childhood infections

The link to the sanitary revolution may be correct, but, if the OF mechanism is also correct, the likely explanation is that these changes have also inadvertently reduced exposure to our Old Friends which occupy the same habitats.



The Health Revolution: Decline in Infant Mortality. Massachusetts: U.S. Bureau of
istics of the United States Colonial Times to 1970, National Center for Health Statistics, *Health*

Dietary changes and microbial content of diet

Modern western diets have been shown to exert profound effects on human gut microbiota.

Whilst **microbiological quality of food has improved**– e.g. eliminating harmful organisms - at the same time we have inadvertently also eliminated Old Friends microbes from our food.

Changes in our dietary habits e.g. (consumption of animal fat versus carbohydrates) have led to changes in types and balance of microbes in our gut.

Child birth, breastfeeding and social contact

Caesarean delivery has been linked to a greater tendency to develop allergic disorders, leading to suggestions that transfer from the bacterial microbiota of the birth canal, in addition to greater exposure to faecal organisms, during **natural childbirth** is important in the early colonisation of the baby's gut

Data consistently shows that **children from large families** are at lower risk of allergies; larger families give more opportunity for sharing gut, skin and respiratory microbiota, for instance by close contact

Can breastfeeding help?

Studies have shown that **breastfeeding for 6 months** or more is protective against allergies.

Exposure to the natural environment

Reduced exposure to important microbial species has also occurred because **of reduced contact with our outdoor environment** and the huge diversity of microbial and helminth (worms) species which it contains. Urbanisation has accelerated loss of exposure to the natural environment. We now spend up to 80% of our time indoors

Studies show:

Studies consistently show that exposure to a farm environment in early life can protect from asthma. The composition of the human commensal microbiota depends on input from the natural environment.

Studies in Finland show that the skin microbiome from individuals living close to agricultural land was more diverse than from those living close to urban centres, and was associated with reduced atopic sensitisation.

Could antibiotics be involved?

Antibiotic usage shows a good temporal fit

- Increasing antibiotic use since 1950s
- Steep rise in allergies from 1970s

Epidemiological studies show that antibiotics may be a risk factor for allergies, particularly excessive use by pregnant mothers or young babies

- Evidence of a link for asthma, cow's milk allergy, IBD, eczema

Antibiotics may alter our interaction with microbes leading to reduced diversity of human gut microbiota

Tests show

Although there is concern about possible confounding of epidemiological studies, studies with humans and mouse models now support this concept.

They show mechanisms by which reduced microbiota diversity can be associated with development of inflammatory disease

Are we too clean for our own good?

What are the origins of this idea?

In proposing the hygiene hypothesis, Strachan suggested that lower incidence of childhood infections could explain the 20th century rise in allergies. This was based on studies showing that larger family size appeared to protect against hay fever.

Strachan suggested that smaller families provided insufficient microbial exposure because of less person to person spread of infection – but also because of "*improved household amenities and higher standards of personal cleanliness*"

From this the notion that "we have become too clean for our own good" has arisen

Respiratory infections can actually increase allergy risks

There is now evidence that childhood infections, far from protecting, actually increase the risk of allergies

Experts agree

Most experts now agree that the "hygiene" hypothesis is a misnomer.

Whilst the link between microbial exposure and inflammatory disease is most probably correct, the idea that children who have more infections are less likely to develop allergies is now largely discounted.

This means that allergies are not the price we have to pay for freedom from infectious diseases

What is the reality?

Home and personal cleanliness

If home and personal cleanliness contributes per se, its role is likely to be small relative to the other factors.

A key point may be that the microbial content of modern homes has altered because mostly our homes now interact with urban environments. These lack the diverse range of microbes found in rural environments and are populated by people with different and less diverse human microbiota.

This means we now interact with an altogether different and less diverse mix of microbes relative to earlier generations which were largely rural.

What about personal cleanliness?

In his early proposition Strachan suggested that, "*higher standards of personal cleanliness*" could also be an underlying cause of reduced microbe exposure

The entire skin surface has about one million resident bacteria per cm^2; numbers vary from 1,000 per cm^2 on forearms to millions per cm2 on underarms.

Our habit of bathing/showering, shampooing have increased since 1940s and 50s. Bathing and showering removes many microbes from skin but are rapidly replaced

Whether, or to what extent, skin microbiota might contribute to the OF mechanism has not yet been studied

Research shows:

Even the cleanest-looking homes are full of bacteria, viruses, fungi, etc.

Routine weekly cleaning has no sustained effect on microbe levels

We cannot create a "sterile" home - microbes are constantly replaced via dust, air, body flora, pets, contaminated foods etc

Helminths (worm) infections are now relatively rare in UK - up to 1950s , 50% children were infested with pinworm

Does cleanliness matter?

What is often forgotten is that the relationship between household or personal cleanliness and development of allergies has never been properly investigated or established.

2002 Study of personal cleanliness

A n analysis of data from the UK ALSPC cohort study of children born in 1991/2 showed association between parent-reported frequency of hand and face washing, showering and bathing at 15 months and wheezing and eczema at 30-42 months, but this has not been confirmed in other studies

From the first study, published in 2015, to directly evaluate this issue, Erika von Mutius, a highly respected researcher in this field, concluded – No. “Development of allergies and asthma is not related to cleaning activities”.

2015 Study of home and personal cleanliness

von Mutius and colleagues studied a group of 399 families . The study showed:

- Bacterial exposure in house dust was associated with reduced risk of childhood asthma and allergies
- Personal cleanliness, such as washing hands, and home cleanliness were objectively reflected by dust parameters in homes

However, neither personal nor home cleanliness were associated with protection from asthma and allergies.

Is microbial exposure the only factor involved?

It is now clear that for any individual, the risk of developing CID depends on many other factors - in addition to microbial exposure.

These include diet (including vitamin D deficiency), pollution, climate change, less physical activity, obesity, socioeconomic factors and stress.

All of these can amplify the immunoregulatory deficit resulting from the changes to our human and microbial environment

Genetic predisposition is also a risk factor.

Why don't we all suffer from allergies etc?

This may explain why we do not all suffer from these diseases. It is likely that we all still get some of the microbe exposure we need.

Whereas for some people this is sufficient, for others it is not.

In these individuals, allergies and other chronic inflammatory diseases (CIDs) may be triggered, when one or more of the other factors cause further dysregulation of the immune system.

How can we reverse the trends in Chronic Inflammatory Diseases?

Therapeutic approaches are being investigated, but are as yet at an early stage.

Using probiotics (drinks or foods) to restore exposure depends on identifying the right microbes

Lifestyle changes which could increase microbial exposure include :

- encouraging natural childbirth,
- sustained breast feeding,
- more physical interaction between siblings,
- more sport and other outdoor activities.

Public Health considerations

Relaxing standards of water, sanitation and hygiene have no guarantee of success and would only serve to increase infectious disease risks.

Encouraging us to abandon cleanliness and hygiene is not the answer to restoring our microbial exposure needs.

Future prospects

With so many factors involved, a single “breakthrough” solution is unlikely. Success will be a slow process, using emerging data to try out new forms of treatment or lifestyle change strategies

Why is hygiene still so important?

At the turn of the C19th, people still lived in constant fear of killer infectious diseases. Hygiene was recognised as vital to reducing risks

Around the 1950s, access to antibiotics and vaccines, clean food and water, toilets and sanitation lulled people into believing that infectious diseases were no longer a real threat. Attitudes to hygiene became more relaxed.

The idea, prevalent at the time, that infectious disease would soon become a thing of the past no longer holds

With rising concern about antibiotic resistance, emerging pathogens etc, we now realise that hygiene is still a cornerstone in the fight against infection in a crowded and mobile world.

Infectious diseases circulating in the community continue to take a heavy toll on health and healthcare systems

Hygiene is an important contributor to global sustainable health

Hygiene-related disease in the home and community

Food-related, waterborne, and non-food-related intestinal diseases remain at unacceptable levels, despite the fact that food borne infections are largely controllable through good food and kitchen hygiene. WHO estimate that about 31% of reported food-borne outbreaks occur in private homes**.**

Salmonella is estimated to cause around 38,000 cases in the UK/year. For ***Campylobacter*** this number is 600,000.

Norovirus affects an estimated 3 million in the UK and 20 million in the US: the majority of cases are spread from person to person via aerosols, hands and surfaces

Respiratory infections remain common: A German study of 1,314 children recorded an average of 21.9 respiratory infections by the age of 12 years, with up to 11 episodes a year . **Good respiratory hygiene** can limit spread of respiratory infections, most particularly colds, but also influenza.

Emerging infections

New pathogens (including antimicrobial resistant strains) are continually emerging. As soon as we get one under control another emerges

Emerging infections in recent years include new agents/strains:

- SARS, Influenza, avian flu
- E.coli O104
- Ebola

In response to the threat of emerging pandemic strains such as influenza, hygiene is now seen as an important first line of defence to contain the disease before vaccines or treatments become available

ID risk in the community is increasing

- The proportion of “at risk” people with reduced immunity to infection, is currently estimated at around 20% in the European community and US, and is likely to increase.
- It includes many who are otherwise considered healthy – the elderly (over 65), the very young, pregnant mothers etc.
- It also includes those with underlying disease: e.g. HIV/AIDS, diabetes
- Hygiene needs do not differ significantly from those which apply to healthy people; it is just that the risks of infection from poor hygiene are greater for “at risk” groups

Did you know?

Prior to the 1980s organisms such as Campylobacter, E. coli O157, legionella and norovirus were largely unheard of

We live in an increasingly crowded and mobile world where new infectious agents and antibiotic resistant strains spread easily and quickly

At risk groups

In the UK, at risk groups living at home and in the community includes the 300,000+ diagnosed annually with cancer and 91,000+ living with HIV .

But it is the elderly that make up the largest numbers of the “at higher risk” population

Home Healthcare

Increasingly healthcare is being delivered at home and in the community. This arises from e.g.

– shorter hospital stays
– home-based treatments such as chemotherapy, dialysis etc

Much of this healthcare is delivered by family members who thus require a good understanding of hygiene

This includes protection from intestinal and respiratory infections (i.e food hygiene and respiratory hygiene), as well as protection from infections associated with their particular condition

Government policy

Governments are now emphasising infection prevention as a means to reduce health spending.

Increased homecare is a favoured approach, but gains are likely to be undermined by inadequate infection control at home.

Antibiotic resistance

Tackling antibiotic resistance is a global priority which involves home and community as well as hospitals. Hygiene is now seen as a central strategy to reducing antibiotic resistance :

Firstly, by reducing the burden of infectious diseases, hygiene can reduce the need for antibiotic prescribing, which is the major underlying contributor to antibiotic resistance

Secondly, infection control measures are important to reduce spread of antibiotic resistant infections in the community.

Thirdly, as persistent nasal , gut or skin carriage of resistant strains increase in the healthy population, the risk of resistant infections in both hospital and community increases

Prevalence of antibiotic resistant strains

A 2012 UK study of 732 healthy people in the community showed that 11.2% were carrying antibiotic resistant ESBL strains in their stools.

A significant proportion of healthcare infections are “self infections” from our own body flora

A Call for Action

Taken together these issues indicate a need for greater investment in prevention strategies such as vaccination programmes and hygiene which are now seen as the most sustainable approaches to containing the burden of infectious disease.

Until now the emphasis has been on prevention of infections in hospitals. Healthcare workers increasingly recognise that reducing infection in healthcare settings cannot be achieved without also reducing the circulation of pathogens such as norovirus, MRSA etc. in the community.

As infection control in healthcare settings improves, hygiene in home and everyday life settings is being exposed as the weak link in the chain?

Developing the right sort of hygiene

Two fundamental questions now need to be answered:

"How can we develop an approach to hygiene, which reconnects us with the necessary microbial exposures, whilst also protecting us against infectious diseases? "

The answer is to promote "targeted hygiene"

How do we change public understanding about the difference between "cleanliness" (absence of visible dirt) and "hygiene" (protecting against infectious diseases)

This is a real challenge

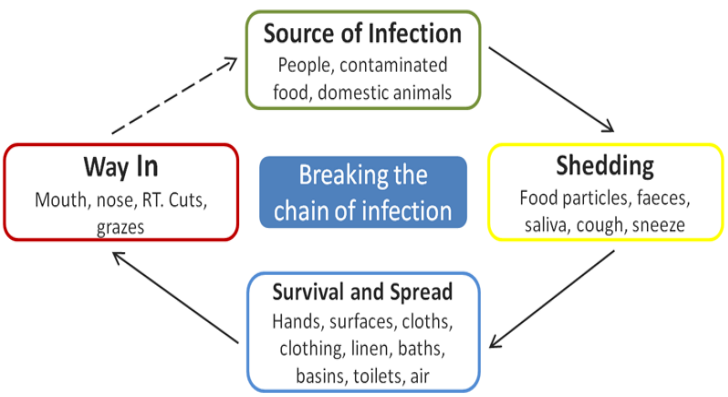
What is targeted hygiene?

Targeted hygiene means knowing the "critical points" in the chain of infection transmission, and using hygiene measures at these points to stop pathogens from spreading further

It makes more sense if we know where harmful microbes (pathogens) start from

- Pathogens mostly come from people, contaminated food and pets in the home
- mostly pathogens use the environment only as the means to spread
- although some can set up home in places where there is dirt, moisture and warmth.

"Getting rid" of the germs from our homes is impossible. Hygiene is the ongoing battle to prevent harmful microbes from spreading i.e. to break the chain of infection



What are Germs?

When someone talks about germs we usually go "yuck" – but be careful – it's often used to mean any type of microbe – including the "good guys" – very confusing!

What are the critical control points?

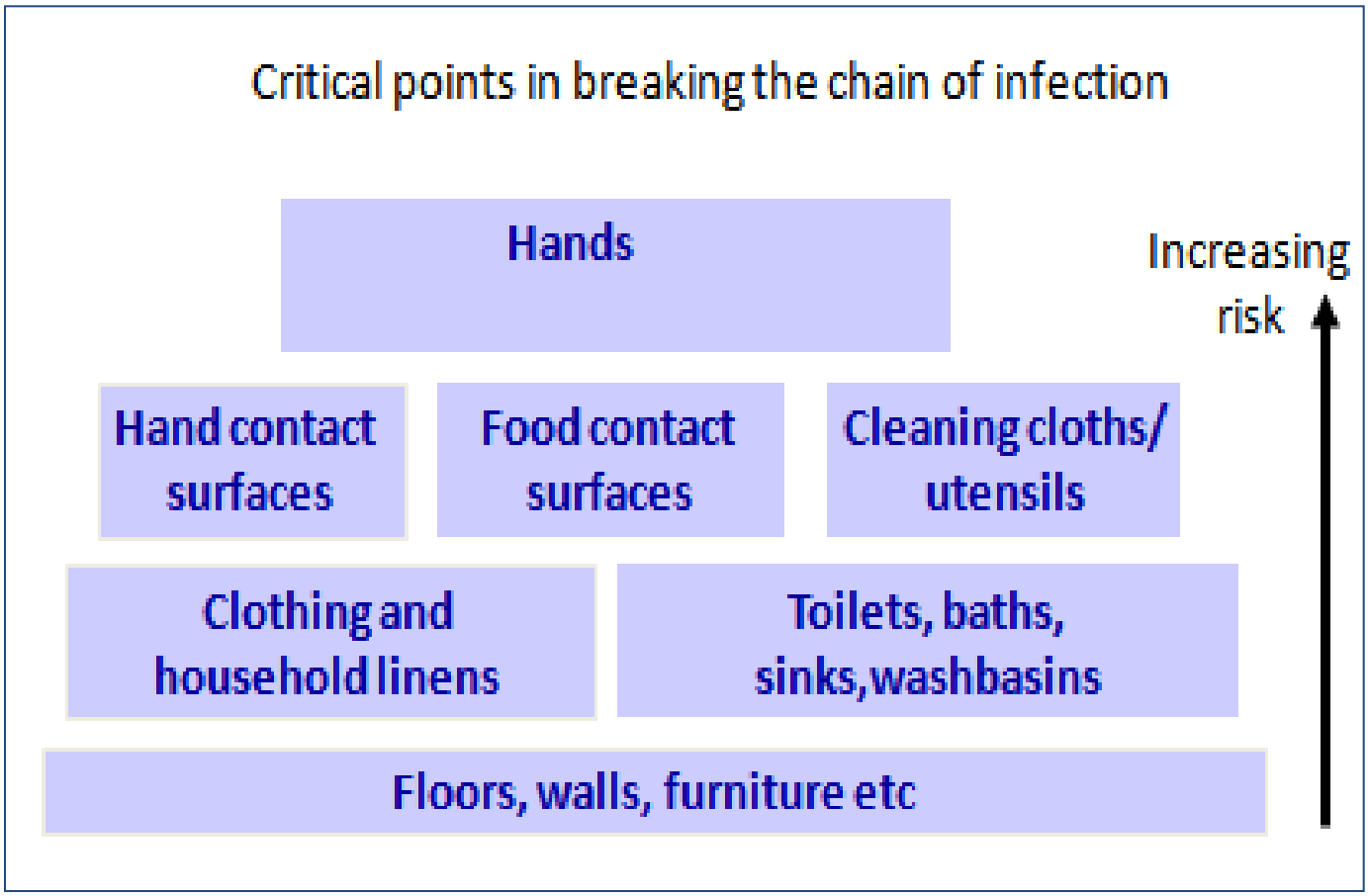
Critical control points for targeted hygiene are:

a) Sites and surfaces where pathogens are most likely found
b) Sites and surfaces which facilitate spread of pathogens

Although this is a useful “rule of thumb” ranking, it is not constant

Risk may increase where someone at home is infected or more vulnerable to infection

- e.g. risk from the toilet increases if someone has norovirus infection
- e.g. risk from laundry increases if someone is infected with athletes foot



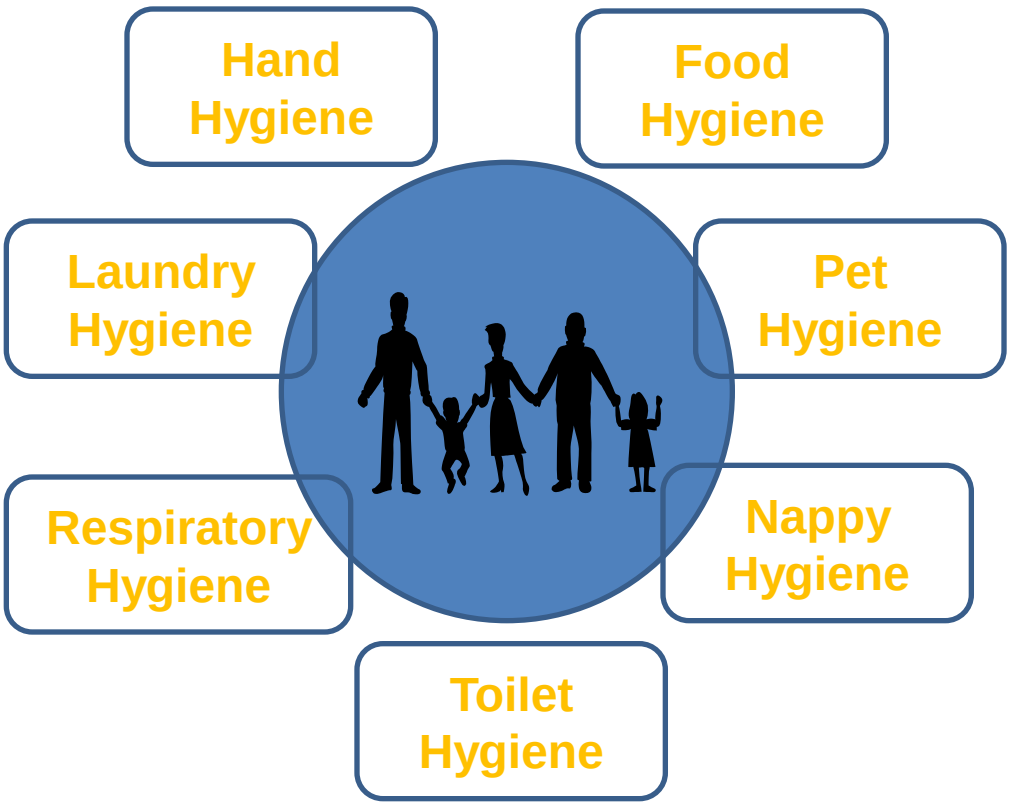
Microbes are found on all sites and surfaces, but most are non-harmful

Explaining targeted hygiene to the public

Telling the public about “critical control points” is too abstract and unhelpful because it gives no indication of “when” it is necessary to apply hygiene practices

It is better illustrated by talking about daily life tasks and situations which they can relate to and which combine to protect them from infection

To know when to act - it’s always important to be aware of where the germ danger is coming from



Keeping our homes clean i.e. dirt free does not stop spread of germs, but it helps because germs don’t survive well in clean dry places

Some examples of targeted hygiene practices

Food Hygiene – Main source is raw food . Targeted hygiene is:

- Safe cooking, safe storage AND

- Preventing cross contamination via **hands, surface and cloth** immediately after handling raw foods/before handling ready to eat foods

Respiratory hygiene **Source is i**nfected people. Targeted hygiene is:

- Catching snot & sneezes etc into a handkerchief/tissue,
- Disposing of tissues etc safely
- then washing hands
- Knowing the virus spreads via hands & surfaces as well as air

Hand hygiene is central to all hygiene practices. Infection occurs by touching the mouth, cuts, wounds, nose & eyes with contaminated hands.

Toilet hygiene: Source is "poo" from infected & healthy people. Targeted hygiene is:

- Wash hands after toilet visits
- Keep toilet clean – Inc. touch surfaces (flush handle, lid etc.)
- Clean and dry cleaning utensils after use
- Wash hands after cleaning toilet

Laundry hygiene: Source is people, food, domestic animals. Targeted hygiene is:

- Laundering risk items using wash cycles that effectively remove microbes &prevent transfer to other items in wash load
- Wash hands after handling soiled laundry

How do we change public understanding?

By dispelling misconceptions about the difference between “cleanliness” (absence of visible dirt) and “hygiene” (protecting against infectious diseases)

By promoting a more positive approach to hygiene

Dispelling misconceptions about hygiene & cleanliness

The public have a lot of misconceptions about cleanliness (absence of dirt) and its relationship to hygiene (preventing spread of infection). For example:

- The terms “hygiene” and “cleanliness“ are used interchangeably to mean “absence of dirt, social acceptability, freshness” but also “infection prevention practices”.
- People assume that dirt is where germ threats are most likely
- People think that if a surface looks clean it is also “germ protection” clean
- People think that if our home has been cleaned all the germs are eliminated
- People don’t distinguish between “aesthetic” cleaning i.e. making things look clean, and “germ protection” cleaning i.e. hand hygiene, food hygiene, toilet hygiene etc.
- Instead of saying “we have become obsessed with cleanliness”, it would be better to say “we have become afraid of getting dirty”
- We think of “germs” as disgusting and dangerous , but we often use this word to refer to any type of microbe - the good guys (our Old Friends) as well as the bad guys

Public confusion and misconceptions

The public are also confused by conflicting stories in the media, some of which warn against the risk of infectious disease and others warn against the “dangers” of hygiene and cleanliness

Promoting a more positive approach?

We need to replace old ideas about the so called hygiene hypothesis with positive messages by

Dismissing statements about "modern obsession with cleanliness, living in sterile homes" and so on as the root cause of allergies etc.

Pointing out that the hygiene hypothesis is a misnomer - relaxing "cleanliness and hygiene" would not reverse the trend in allergies etc. – it would only increase infectious disease risks.

Stressing what ARE the major causes of "Microbiome depletion"

Talking about appropriate lifestyle changes to re-engage with our Old Friends: i.e natural childbirth, breastfeeding, avoiding antibiotics, outdoor activity etc.

Stressing that getting dirty is healthy, but hygiene is vital in times & places that matter

The fundamental question is

"How can we develop lifestyles, together with health policies, which reconnect us with the necessary microbial exposures, whilst also protecting us against infectious diseases?"

In view of current global concerns about infectious diseases and antibiotic resistance, and our growing understanding of how these issues can be tackled through better home and everyday life hygiene, there is an urgent need to ensure that misconceptions about hygiene and cleanliness are replaced with clear understanding of the basic principles of hygiene

Do we need germ exposure to keep our immune system strong?

Immunity to infectious diseases

A quite separate issue from the Old Friends Mechanism (so-called hygiene hypothesis) and allergies etc. is the popular notion that clean modern lifestyles may be weakening the immune system, making us more susceptible to infectious diseases.

If this were the case, infectious disease statistics – particularly respiratory infections like coughs, colds and flu – would be rising rapidly, but they are not.

Although acquiring a normal body microbiota during, and in the first months after, birth is critical to developing the immune system, there is currently no evidence that "regular" infections during childhood and adulthood are important to keep our immune system "strong" and boost our immunity to infection.

People tend to assume that regular exposure to dirt and germs is important so children build up a strong immune system to fight infection despite the fact that there is no evidence for this

How do we build immunity to infection?

The way to develop **specific immunity** to a particular diseases (e.g. chicken pox, measles, flu) is to catch that disease or be vaccinated against it. We are also probably exposed to small doses of various pathogens in our daily lives - large enough to develop immunity but too small to overwhelm the immune system and make us ill.

However, catching a dose of flu or a cold does nothing for immunity to Campylobacter or E. coli, or vice versa. So it's not true that catching lots of infections boosts our general immunity against all infections.

Factors which reduce our general immunity to infection are poor lifestyle and poor health – poor nutrition, malnutrition, excessive alcohol consumption, drug abuse, stress, etc.

The best way to build general immunity to infection is through a healthy balanced lifestyle

Read more about the immune on the following pages

The immune system, how does it work?

Introduction

To understand both:

- the role of the immune system in protecting us from infectious disease
- the inappropriate overreactions of the immune system which cause allergic and autoimmune diseases

requires some understanding of how the immune system works. The following is a simplified explanation of what, in reality, is a very complex system.

The immune system is a network of organs, cells, antibodies and chemicals. Its basic function is to prevent and eliminate infections. There are 2 parts to the system – innate and acquired immunity.

Innate immunity - the first line of defence against invasion.

This system is always present in the body and defends us against any foreign agent regardless of type, species etc. i.e. it is non specific

Acquired immunity - the second line defence system against infection which creates a response specific to the invading substance.

When novel substances enter the body, they are recognised as 'foreign'. The body needs to be able to recognise the difference between its own tissues and these foreign invaders. This 'learning' process is particularly important in the early stages of life, e.g. in the womb and shortly after birth

Substances recognised as foreign by the immune system **(bacteria, viruses, fungi, parasites , pollen, dust mites etc)** are called **antigens**

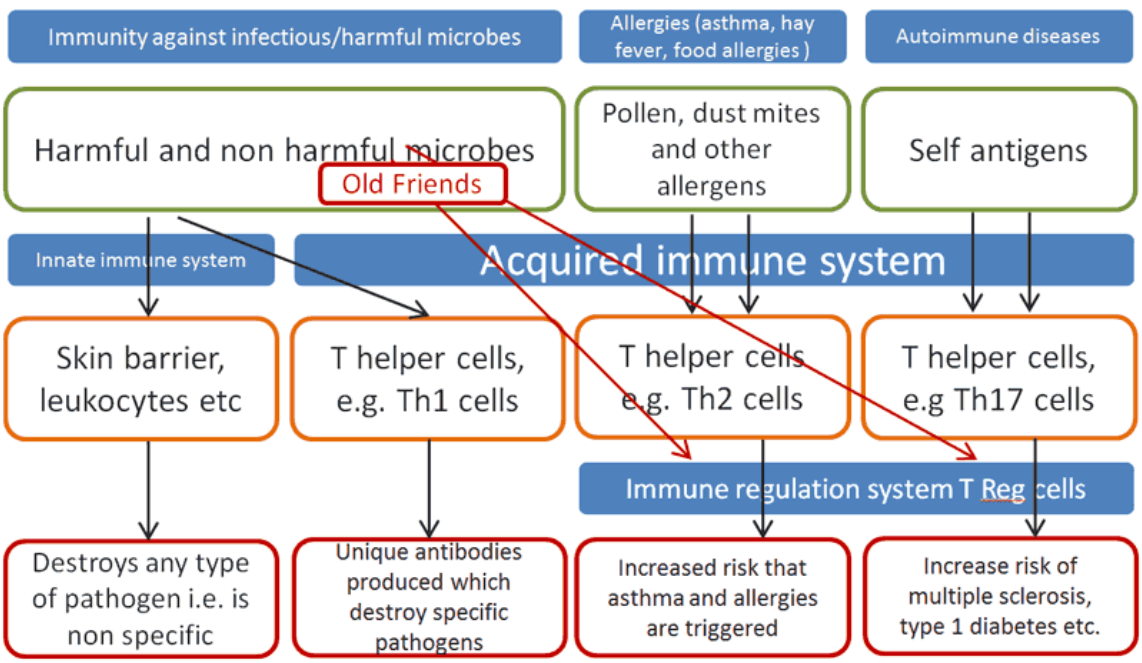
Immune functions relevant to this resource

The four immune functions relevant to this resources are:

1. General immunity to infection
2. Specific immunity to infection
3. Allergies and other inflammatory diseases
4. Immune regulation & old friends mechanism

In the diagram below we have attempted to summarise these systems in diagrammatic form.

A key thing to note is the difference between the immune systems which protect the body from infection and the Old Friends Mechanism whereby the immune system is protected against overreaction to pollen etc which cause allergies by microbial exposure



1. General immunity to infection

This is the function of the **innate immune system** which defends us against any foreign agent regardless of type of species.

Key components include:

- **skin and mucous membrane** (mouth, nose etc.) which act as physical barriers preventing access of microbes to underlying tissues.
- A variety of cells (such as **leucocytes and natural killer cells**) which circulate in the blood stream and engulf and eliminate microbes, pollen or dust etc. that succeed in entering the body.
- **Plasma proteins** that circulate in the bloodstream or lymphatic system

There is no evidence that the innate immune system requires “practice” (e.g. constant exposure to foreign agents) to keep it strong)

Factors which reduce general immunity are poor lifestyle and poor health – poor nutrition, malnutrition, excessive alcohol consumption, drug abuse, stress, etc.

2. Specific Immunity to infection

If the initial innate response to a foreign invader (such as a disease -causing pathogen) fails, the **acquired immune system** takes over.

The acquired system is extremely complex and consists of many interrelated components. Two key elements are

- **B-cells** which produce specific proteins called **antibodies** that neutralise the invader
- **T-cells** that attack the invader or regulate responses of other immune cells

There are many different **T-cells**, but important groups are:

- **Killer cells** destroy pathogen-infected cells and other 'foreign' cells
- **Helper T-cells** (Th) are regulators of cellular immunity. There are many types of Th cells, but the types important to this learning material are **Th1, Th2 and Th17** cells

When pathogenic bacteria, viruses or fungi (each consisting of many specific antigens) enter the body, B cells respond by producing antibodies (immunoglobulins) specific for each antigen.

There are many different types **of immunoglobulins**, but in response to infection two important types are **IgG and IgA**

Th1 helper cells 'assist' some of the B cells to become **plasma cells**

Plasma cells rapidly divide and secrete more antibodies that neutralise invading pathogens, until the infection is controlled.

Vaccination

After recovery from an infection, the body retains some of the B and T lymphocytes (known as memory cells) which persist in the blood and lymph systems. If re-exposed to the same antigen threat, the memory cells mount a strong rapid immune response

This is the basis of vaccination e.g. flu virus, treated to destroy their disease-causing properties but not their antigenic properties, are injected to induce permanent resistance to the strain of flu

2. Specific Immunity to infection – continued

Specific immunity – the cellular system

When a pathogen (consisting of many specific antigens) enters the body, the **cellular immune system** also plays in important role in controlling infection.

It includes a wide variety of cells but **T-cells** (listed on the previous page) are the type that are relevant to this resource

There are many different T-cells, but important groups are:

- **Killer T-cells** destroy pathogen-infected cells and other 'foreign' cells
- **Helper T-cells** (Th cells) are key regulators of cellular immunity
    - **Th1 cells** help B-cells to produce antibodies
    - **Th2 cells** help B cells to secrete **IgE**
    - **Th17 cells** play a role in regulating autoimmunity
- **Regulatory T cells (Treg cells)** have an immune regulatory role - see slide s 38 and 40

3. Allergies and autoimmune diseases

Agents such as pollen, dust mites, certain foods etc can act as **antigens** and induce an immune response.

- **Allergic diseases** such as asthma, eczema, food allergies occur when the body overreacts to antigens (also called allergens) such as pollen, dust mites etc causing inflammatory responses such as sneezing and irritation.
- **Autoimmune diseases** such as Type 1 diabetes and multiple sclerosis etc occur when the immune system overreacts against the body's own cells and tissues (self antigens).

The process by which the body prevents itself from attacking its own cells is called **Immune tolerance**.

Allergies – asthma, hayfever, food allergy, excema etc

In response to exposure to an antigen such as pollen, dust mites etc, the allergen binds to the surface of **B Lymphocyte** cells

T lymphocytes (**such as Th 2 cells**) also bind to the antigen and in so doing activate the B cells to secrete immunoglobulin, IgE.

IgE, in turn, reacts with **Mast cells** which release pharmacologically active agents which cause the typical symptoms such as irritation, sneezing, constriction of the airways etc

Autoimmune diseases

Autoimmune diseases such as Type 1 diabetes, inflammatory bowel disease and multiple sclerosis result from a failure of **Immune tolerance** mechanisms found in the normal human body

This leads to production of antibodies or inflammatory agents against the bodies own cells (self antigens) or activation of other types of T helper cells e.g **Th 17 cells** which react with self antigens.

This leads to the tissue injuries and degradation typical of autoimmune diseases

4. Regulation of immune responses

Acquired immunity as described in section 2 of this appendix is vital to protect the body against infectious disease, but these immune responses are potentially dangerous if they are not properly regulated as happens in those who develop allergies and autoimmune diseases

Preventing or limiting inappropriate immune responses, is brought about by T lymphocyte cells called **regulatory T lymphocytes (Treg cells)** that have an 'immune management' role.

Under certain conditions, T reg cells secrete **anti-inflammatory substances** which suppress the helper Th2 and Th17 cell responses leading to downregulation of allergic and autoimmune reactions., thereby avoiding development of allergic and autoimmune diseases

The Old Friends mechanism

In normal humans, T cell secretion of the anti-inflammatory substances that suppress allergic and autoimmune responses is driven by exposure to Old Friends organisms such as helminths, commensal microbiota and environmental saprophytes. (They also help to switch off responses to infections once the antigens have been eliminated).

In the absence of stimuli from these Old Friends, **Treg cells** are no longer adequately induced causing increased susceptibility to "overreaction" leading to allergic and autoimmune diseases.

Over time the body has evolved to distinguish antigens of disease-causing microbes that need to be eliminated, from antigens of the OF organisms that need to be tolerated, but which are still recognised by the immune system and interact with it to drive the Treg responses which prevent allergies and autoimmune disease.

It may be that constant exposure to a biodiverse library of harmful and non harmful microorganisms, and self antigens is necessary for maintaining and constantly evolving our immune regulatory system.

Recommended Publications

Stanwell-Smith R, Bloomfield SF, Rook GA. 2013

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

http://www.ifh-homehygiene.com/best-practice-review/hygiene-hypothesis-and-its-implications-home-hygiene-lifestyle-and-public-0

Bloomfield SF, Stanwell-Smith R, Rook GA. 2013

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

http://www.ifh-homehygiene.org/best-practice-review/hygiene-hypothesis-and-its-implications-home-hygiene-lifestyle-and-public