

Normal Flora

HUMAN MICROBIOME IN HEALTH AND DISEASE



Normal flora has many names :

1. Microbiome
2. Bioneme

Dr. Waleed Al Momani, MLT, PhD

Extra info : microbiome is the microorganisms in a particular environment including the body or part of the body.

- Microbial ecology is the study of the numerous interrelationships between microbes and the world around them. طبعاً هي العلاقات (قابلة للتطبيق) لأنه قد يكون ال
Applicable
Microbe :
 1. Harmful
 2. beneficial
 3. have no effect, nether gain nor loss
- Microbes interact with humans in many ways and at many levels.
- The most intimate association that we have with microbes is their presence both on and within our bodies
All microbes living in or on the human body = normal flora (microbiome)

Symbiotic Relationships Involving Microorganisms

- Symbiosis is defined as the living together or close association of two dissimilar organisms (usually two different species).

- Neutralism
- Commensalism
- Mutualism
- Parasitism

Indigenous Microbiota of Humans

- A person's indigenous microbiota (sometimes referred to as the human microbiome or human bioneme) includes all of the microbes (bacteria, fungi, protozoa, and viruses) that reside on and within that person

The best way to build up microbiome is the actual infection even better than the vaccine

تعريض الطفل للعدوى infection ويصير الseroprevalence تبعه عالي ويزيد قوة الجهاز المناعي هي احسن طريقة لمقاومة الامراض وزيادة الnormal flora

- During pregnancy, the human fetus lives in a remarkably protected and for the most part sterile environment

The normal flora starts from the scratch(zero)

So this means that the fetus has no normal flora when he is still in his mother uterus(the fetus is in sterile environment) بيئة معقمة

The normal flora starts to build up during (delivery or during labor) and for being more exact during passing the birth canal.

- Over the next few years, communities of organisms (microbiota or normal flora form on the surfaces of the skin, nares, oral cavity, intestines, and genitourinary tract. Microbiome takes time like few years to be established

يعني تحتاج الى وقت حتى نستطيع القول ان ال normal flora is in full setup

When normal flora reaches its full setup this means that it become competent.

And this means that it can compete with the non-flora



The birth canal has some organism so this is the first exposure of the baby with the microorganisms.

And the time needed for the normal flora to reach its full setup depends on the exposure (frequency of the exposure).

وقديش هذا البيبي
تعرض للبيئة الخارجية
وقديش تعرض
للمايكروبات.
فكل ما زاد تعرضه زاد
سرعة حصوله على ال
normal flora.



التعامل مع الحيوانات ممكن
يعطيك بعض ال microbes
التي توجد بالحيوانات
المنزلية

Babies with much higher hygiene level slowly Develops normal Flora and this have a negative impact on the baby because as soon as the baby is sick the signs and symptoms is severe because he does not have the first defence mechanism wich is the normal flora



احسن مكان تاخذ منه
الميكروبات هي التربة



The Human Microbiome Project

- 5-year multinational study to analyze the genetic composition (microbiome) of the microbial populations that live in and on healthy adults.

كل جزء من الجسم لديه *normal flora* خاصة فيه

- It is estimated that bacterial cells outnumber human cells in the host by 10 : 1

Not all organs contains microbiome some are organism free
For example circulatory system, brain, heart, lung and kidney or ar
vital organ is organism free

- A recent study estimated the ratio as 1.3:1 (science news: [Vol. 189, No. 3, February 6, 2016, p. 6](#))

- The Human Microbiome Project was launched in 2007 with the collection of samples from the nose, mouth, skin, gut, and vagina from healthy adult volunteers

This project state that the Normal flora has 2 types :

1. Core microbiome : when the majority of the healthy adults has specific bacterial species in a specific site
2. Secondary microbiome : when the minority of the healthy adults has specific bacterial species in a specific site

الفرق بين ال core وال secondary هو ان ال core يلعب دور مهم في صحة الانسان (defence mechanism)

- Bacteria colonizing the gut are different from those in the mouth, skin, and other body sites.
- The greatest taxonomic and genetic diversity was the intestine, and the vagina was the least complex.

المكان الانظف هو المكان الذي يحتوي عادة على تنوع اكبر من
microorganisms ال

- Microenvironments such as different regions of the mouth, gut, skin surface, and vagina also had their own unique microbiome

All the thioglycolate median are found in the oral cavity but not found in the intestine

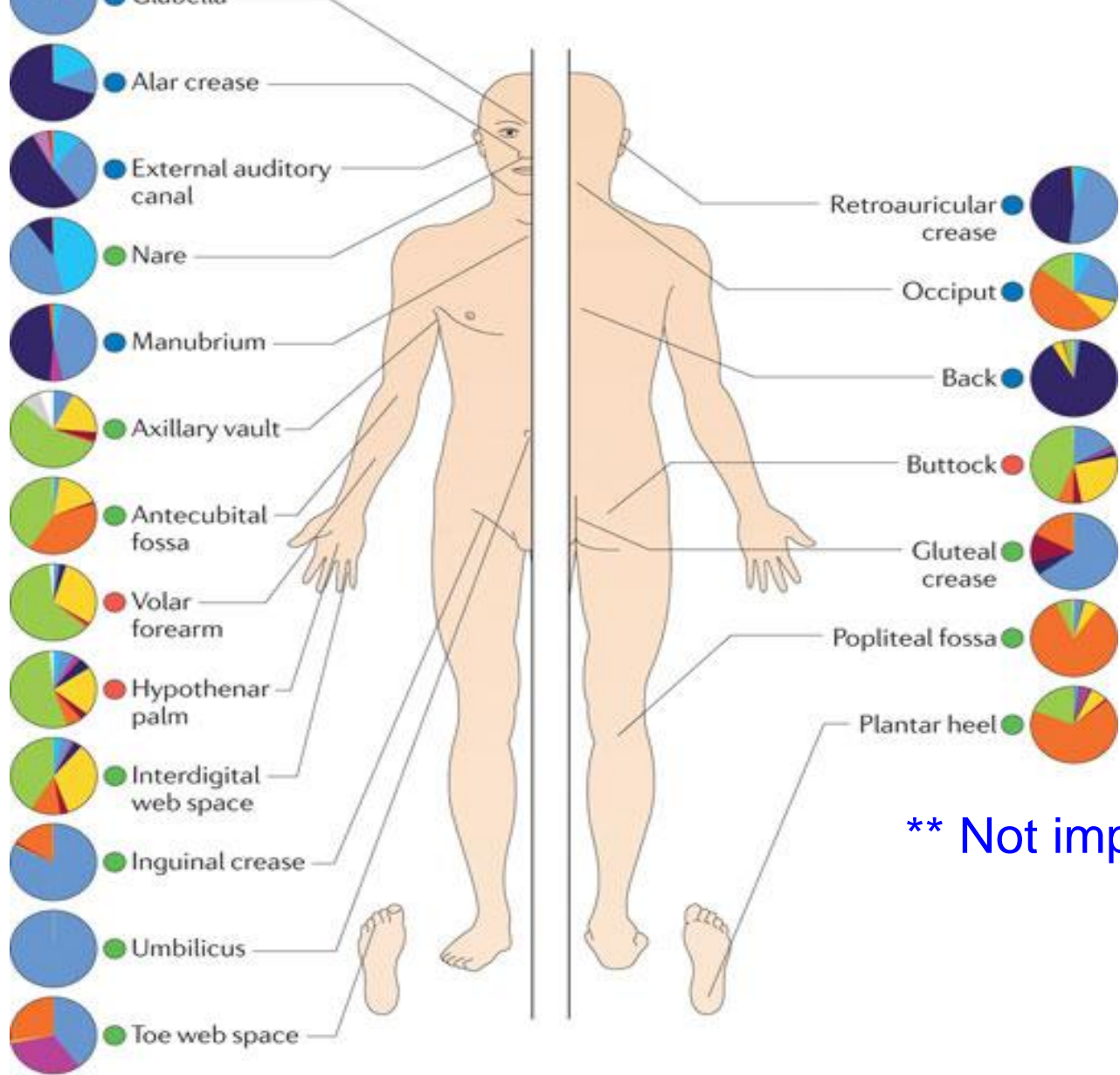
The biggest number of normal flora is found in the large intestine.

In large intestine we only find anaerobe and facultative

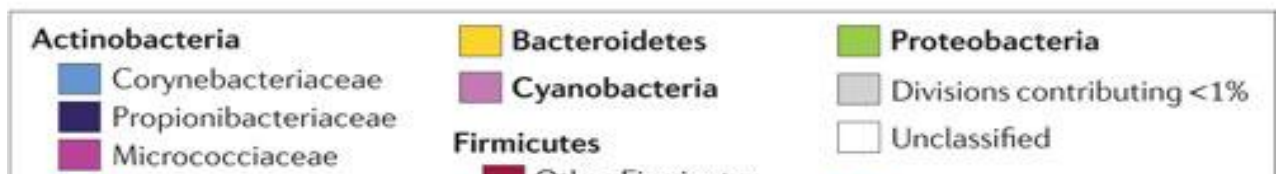
But the biggest diversity for the different types of microorganism is found on the oral cavity because it is the cleanest part of the body and because of the different environment .

Core Microbiome

- Most individuals share a core microbiome, arbitrarily defined as the species that are present at a specific site in 95% or more of individuals.
- The greatest numbers of shared species are present in the mouth, followed by the nose, intestine, and skin, and the fewest shared species are found in the vagina
- Secondary microbiome consists of small numbers of many species that may not be widely shared by individuals



** Not important **



Microbiota of the Skin

Although the skin is the most exposed part of the body it have only few microorganisms that could live on the skin.

- The resident microbiota of the skin consists primarily of bacteria and fungi—as many as 300 different species, depending on the anatomical location
The organisms that are isolated from the skin is the gram positive bacteria especially staphylococcus, etc.
- The most common bacteria on the skin are species of Staphylococcus (especially S. epidermidis and other coagulase-negative staphylococcia), Corynebacterium, and Propionibacterium

Although corynebacterium is anaerobe but it lives in the base of the hair

تعيش في بصيلات الشعر عشان تختبئ من الاكسجين وهي المسؤولة عن حب الشباب

The number and variety of microorganisms present on the skin depend on many factors, such as:

- Anatomical location بعض المواقع في الskin تساعد على النمو وبعضها لا يساعد وبعضها يوجد به نمو كبير .
- Amount of moisture present
- pH The dryness of the skin is an important feature because Bacteria loves wet places and not all types of bacteria could live in dried areas.
- Temperature
- Salinity
- Presence of chemical wastes such as urea and fatty acids
- Presence of other microbes, which may be producing
- toxic substances

Microbiota of the Ears and Eyes

- The middle ear and inner ear are usually sterile, whereas the outer ear and the auditory canal contain the same types of microbes as are found on the skin.

The eyes has an important defence mechanism which is blinking and tears.

its own defence mechanism كل سيستم بجسم الانسان عنده

For example : the lung has defence mechanism which has alveolar macrophage

فهي عبارة عن خلايا مناعية ثابتة على باب الدئة تمنع دخول اي جسم غريب وبتعمله (engulf)

In the liver u will find kupffer cells

And the defence mechanism could be in the form of salt (bile salt) like in the intestine.

And the defence mechanism could also be physical or chemical

For example the urinary system uses 2 ways for the defence mechanism:

1.physical : the urine flush which is emptying the urinary bladder.

2.chemical : the PH, the acidity of the urine decrease the growth of the bacteria

Microbiota of the Respiratory Tract

- The respiratory tract can be divided into the upper Respiratory tract and the lower respiratory tract.
- The Upper respiratory tract consists of the nasal passages and the throat (pharynx).
- The lower respiratory tract consists of the larynx (voice box), trachea, bronchi, bronchioles, and lungs.

The upper respiratory tract is full of microorganisms
But the lower respiratory tract is organisms free

The lung is organism free because of the alveolar macrophages and the Mucociliary Escalator which is the mucus lining.

Microbiota of the Oral Cavity (Mouth)

- The anatomy of the oral cavity (mouth) affords shelter for numerous anaerobic and aerobic bacteria.

The list of microbes that have been isolated from healthy human mouths includes:

Gram-positive and Gram negative bacteria (both cocci and bacilli), spirochetes, and sometimes yeasts, mouldlike organisms, protozoa, and viruses. The bacteria include species of *Actinomyces*, *Bacteroides*, *Borrelia*, *Corynebacterium*, *Fusobacterium*,

Microbiota of the GI Tract

- The GI tract (or digestive tract) consists of a long tube with many expanded areas designed for digestion of food, absorption of nutrients, and elimination of undigested materials.
- Excluding the oral cavity and pharynx, which have already been discussed, the GI tract includes the esophagus, stomach, small intestine, large intestine (colon), and anus.
- Accessory glands and organs of the GI system include the salivary glands, pancreas, liver, and gallbladder.

Although the stomach environment is very acidic but we can still find a specific species of bacteria which is the *Helicobacter pylori*.

هناك البكتيريا عندها القدرة على ان تفرز انزيم اسمه ال urease enzyme والتي برفع الPH بالمنطقة المحيطة بالخلية البكتيرية .

- There is one bacterium—a Gram-negative bacillus named ***Helicobacter pylori***—that lives in some people's stomachs and is a common cause of ulcers.

لو تم قياس الPH لمريض عنده peptic ulcer رح نلاحظها طبيعية
يعني ما حتكون 6 او 5 ، حتكون بالحالة الطبيعية من 1 الى 3 .

- A few microbes, enveloped by food particles, manage to pass through the stomach during periods of low acid concentration.
- Also, when the amount of acid is reduced in the course of diseases such as stomach cancer, certain bacteria may be found in the stomach.

50% of The faecal materials in the large intestine is composed of bacteria.
There is a strong relationship between the healthy large intestine normal flora and the other parts of the body.

مثال على ذلك انو في علاقة بين الـ normal flora في الـ large intestine و الـ mental health

فمعناته كلما ما زادت الـ normal flora زادت القدرات والصحة العقلية

- The colon contains as many as 500 to 600 different species— primarily bacteria.
- Bacteria found in the GI tract include:
Actinomyces, Bacteroides, Clostridium, Enterobacter, Enterococcus, Escherichia, Klebsiella, Lactobacillus, Proteus, Pseudomonas, Staphylococcus, and Streptococcus.
- Also, many fungi, protozoa, and viruses can live in the colon

Microbiota of the GU Tract

- The GU tract (or urogenital tract) consists of the urinary tract (kidneys, ureters, urinary bladder, and urethra) and the various parts of the male and female reproductive systems.
- The healthy kidney, ureters, and urinary bladder are sterile.
- However, the distal urethra (the part of the urethra farthest from the urinary bladder) and the external opening of the urethra harbor many microbes, including bacteria, yeasts, and viruses.

معظم حالات ال urinary tract infection سببها ال normal flora الموجودة بال distal urethra وخاصة عند الناس الي دايمًا ماسكين حالهم بحيث انو ال bladder يكبد بالحجم وبعدين ال normal flora بتدخل على ال bladder الي هي اصلا sterile وبتبدا ال microbial growth وممكن تنتشدر up road يعني بتكون ascending من الاسفل الى الاعلى.

- The reproductive systems of both men and women are usually sterile, with the exception of the vagina
- The microbiota varies with the stage of sexual development.
وجود ال lactobacillus او ال Acidophiles مهم وديد على صحة ال vagina ، اذا مش موجودات بنحكي انو في مرض
- Bacteria found in the vagina include species of Actinomyces, Bacteroides, Corynebacterium, Klebsiella, Lactobacillus, Mycoplasma, Proteus, Pseudomonas, Staphylococcus, and Streptococcus
The normal flora in the vagina is age dependent, and the age depends on hormonal changes, and the hormones of the female changes from prepuberty to puberty to postpuberty.

Thus hormones determine the PH

فبتالي ال normal flora تعتمد على ال hormones .

Beneficial and Harmful Roles of Indigenous Microbiota

- Certain of our intestinal bacteria are beneficial to us in that they produce useful vitamins and other nutrients
- Microorganisms of the normal flora may aid the host (by competing for microenvironments more effectively than such pathogens as *Salmonella* spp or by producing nutrients the host can use)

Harmful normal flora is the opportunistic organisms.

The normal flora that is found in the oral cavity like streptococcus mutanse

Cause dental caries (تسوس الاسنان)

فاذا ما كان في تنظيف للفم وعناية هذه البكتيريا رح تعمل q build up biofilm matrix وبتبدا النخر بالاسنان

- May harm the host (by causing dental caries, abscesses, or other infectious diseases)
- May exist as commensals (inhabiting the host for long periods without causing detectable harm or benefit).

Microbial Antagonism

- The term microbial antagonism means “microbes versus microbes” or “microbes against microbes”

Microbial Antagonism

1. Competition for nutrition

The normal flora that is permanent resident

invaders source of nutrients ال اسرع من ال
فبتالي ال normalflora بتاخذ ال nutriens ويتحدم ال invaders .

2. Competition for space

The bacteria almost occupies the entire surface so there will be no place or space for the pathogens to attach.

3. Production of antibiotics and bacteriocins.

Many types of bacteria secretes chemicals that can kill other species
For example : the bacteria that is found on the skin (G+) can produce bacteriocin that kills the (G-) bacteria.

Opportunistic Pathogens

- Many members of the indigenous microbiota waiting for the opportunity to cause infections
- If the normal microbiome characterizes health, alterations in the microbiome can signify disease, a relationship we are only beginning to understand.

- Microbiome research has introduced a new concept—disease caused by a community of organisms rather than a single species of bacteria
- We are now at the forefront of a new era of defining infectious diseases.

Biotherapeutic Agents

بسببها بنحافظ على ال normal flora

Indigenous microbiota is upset by:

- Antibiotics, other types of chemotherapy, or changes in pH, many complications may result.
- Bacteria and yeasts that are ingested to reestablish and stabilize the microbial balance within our bodies are called biotherapeutic agents or probiotics.

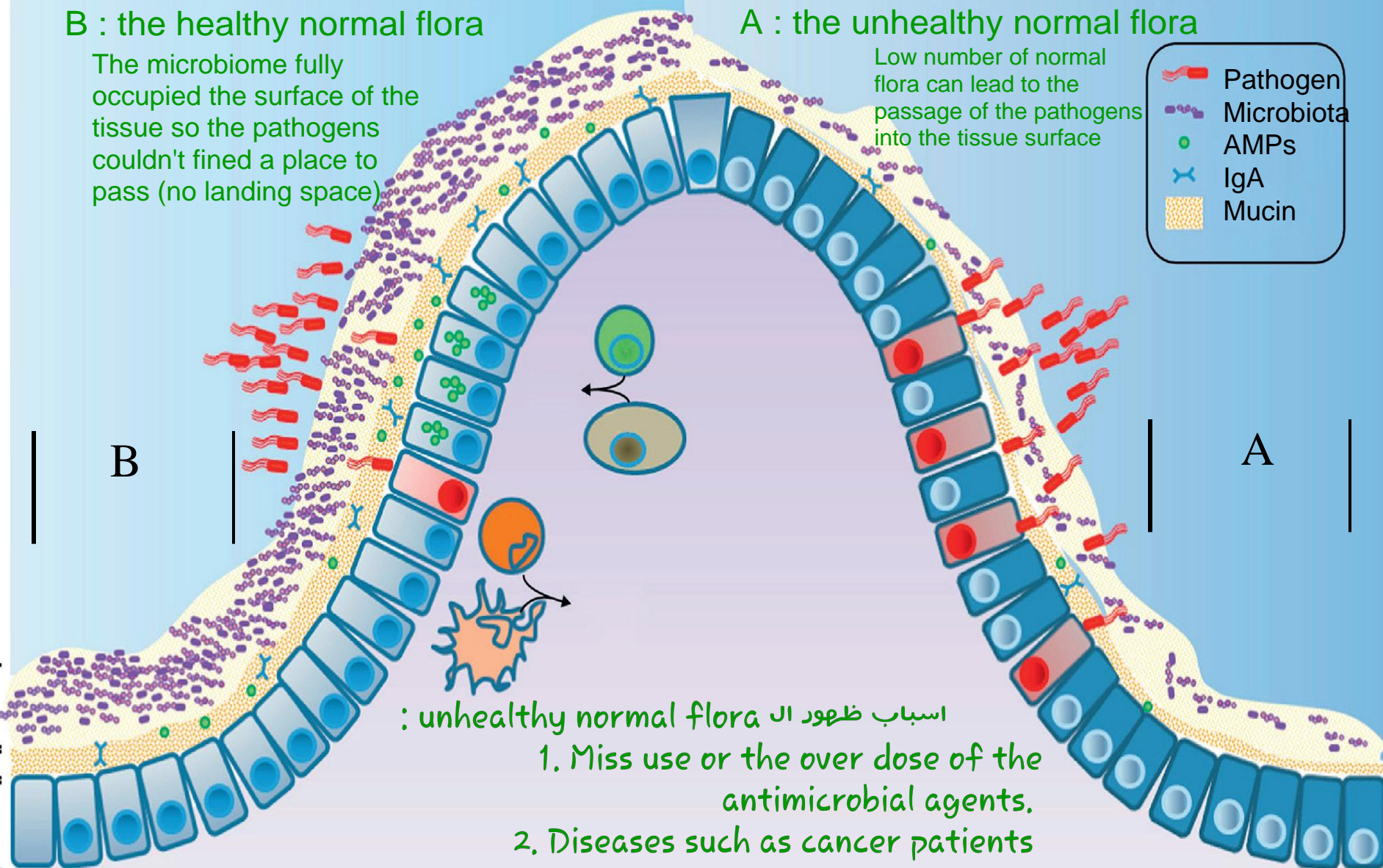
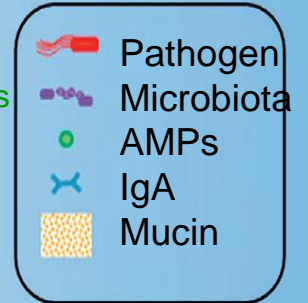
- Disruption of the normal microflora (commonly referred to as **dysbiosis**) can lead to disease by the elimination of needed organisms or allowing the growth of inappropriate bacteria
- Shift in the skin microbiome means the change from G+ to G-
- Shifts in the skin microbiome → wound infections and dermatitis. And skin abscess
- Alteration in the vaginal microbiome → vaginitis.

B : the healthy normal flora

The microbiome fully occupied the surface of the tissue so the pathogens couldn't find a place to pass (no landing space)

A : the unhealthy normal flora

Low number of normal flora can lead to the passage of the pathogens into the tissue surface



اسباب ظهور ال unhealthy normal flora :

1. Miss use or the over dose of the antimicrobial agents.
2. Diseases such as cancer patients

Microbial Communities (Biofilms)

Biofilms have high resistance to antibiotics

Because there is a strong network

- In nature, microbes are often organized into complex and persistent communities of assorted organisms called biofilms.
- Biofilms endocarditis, cystic fibrosis, middle ear infections, kidney stones, periodontal disease, and prostate infections.

Synergism (Synergistic Infections)

Synergistic infection=poly microbial infection=super infection=mixed infection

- Sometimes, two (or more) microorganisms may “team up” to produce a disease that neither could cause by itself. This is referred to as synergism or a synergistic relationship.

: synergistic infection مشكلة

1. In the diagnosis : صعب تحديد الانواع لانه بتكون مجموعة مشكلة من الانواع

2. In the treatment : بدل ما استخدم مضاد حيوي واحد لازم استخدم مجموعة مضادات

- The diseases are referred to as synergistic infections, polymicrobial infections, or mixed infections.

Soil Microbes

A variety of human pathogens live in soil, including:

- Various *Clostridium* spp. من اخطر انواع ال anaerobe
لانها تسبب مرض ال Tetanus
- The spores of *Bacillus anthracis*
- Various yeasts

The types and amounts of microorganisms living in soil depend on many factors, including:

- The amount of decaying organic material,
- Available nutrients,
- Moisture content,
- Amount of oxygen available,
- pH, temperature,
- The presence of waste products of other microbes.

Infectious Diseases of Farm Animals

zoonotic diseases : the diseases that is transmitted form the animals to humans

And this process is (1 way)

- Farmers, ranchers, and agricultural microbiologists are concerned about the many infectious diseases of farm animals— diseases that may be caused by a wide variety of pathogens (e.g., viruses, bacteria, protozoa, fungi, and helminths) 70% of the human diseases originated from animal

معظم مشاكل ال *resistance* جاي من الحيوانات وليس من الانسان لانو احنا بناخذ بقايا ال

antibiotics الموجودة باللحمة والموجودة بالحليب وغيرها

- Microbes cause many diseases of farm animals, wild animals, zoo animals, and domestic pets.

استهلاك المضادات الحيوية في الانسان فقط 30% اما بالحيوان 70%

ويستخدموه مش لانو الحيوان مريض بالعكس يستخدمه عشان ال *prevention* عشان ما يمرض

بس بالمقابل لديه *very bad impact* على حياة البشر .