Lecture # 2

Normal microbial flora or Normal Microbiota or Normal Flora or Microbiome

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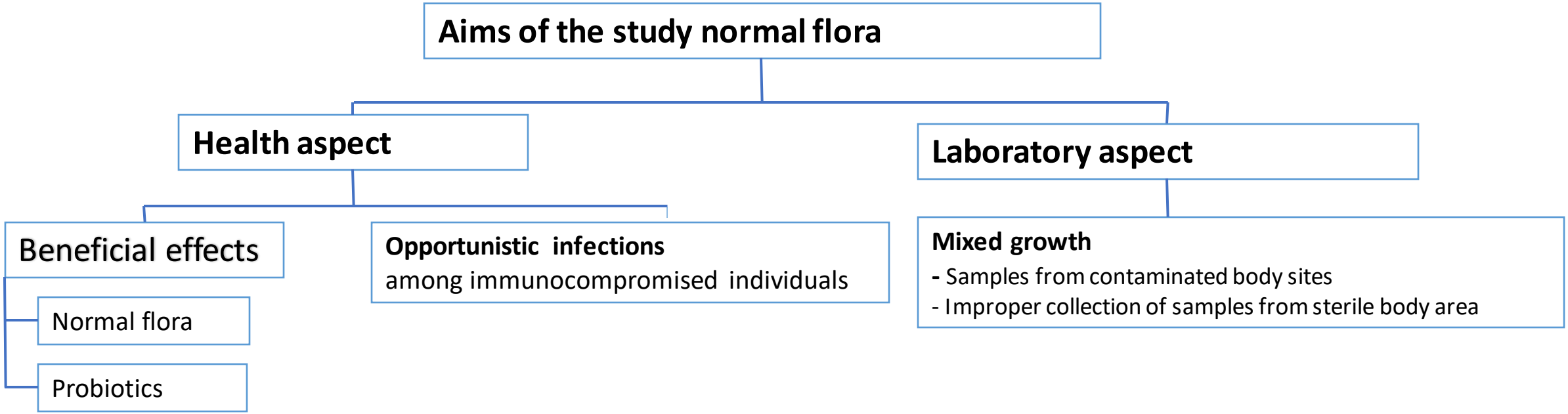
What is the importance of this subject?

From the health point of view, we always want to maintain normal flora as part of the our non-specific immunity as well as used as adjunctive treatment in certain conditions as probiotics.

Certain infections are caused by opportunistic pathogens mainly among immunocompromised individuals.

From diagnostic point of view, bacteriologist must be able to differentiate between contaminant bacteria growth and real pathogens. This is the challenge for diagnosis of infections from contaminated body sites.

Formulate a schematic draw to previous slide (slide #2)


Aims of the study normal flora
Health aspect
Laboratory aspect
Beneficial effects
Normal flora
Probiotics
Opportunistic infections
among immunocompromised individuals
Mixed growth
- Samples from contaminated body sites
- Improper collection of samples from sterile body area

Definition

- **The population of microorganisms that inhabit the skin and mucous membranes of healthy normal persons and live in mutualistic relationship.**

Which m.os can be normal flora
A-Bacteria
B-Protozoa
C-Viruses
D- Helminthes
E-Fungi

Do you know that the total number of normal flora outnumbered our cells by a factor of 10 (10^{13} versus 10^{14})

Scientists believe that the genetic composition of the normal flora (Microbiome) may have a role in the health and diseases of human and another describe the second brain in the gut of human.

Types of Normal flora

(1) Resident normal flora consists of relatively fixed types of microorganisms regularly found in a given area at a given age; if disturbed, it promptly reestablishes itself.

(2) Transient Normal flora consists of nonpathogenic or potentially pathogenic microorganisms that inhabit the skin or mucous membranes for hours, days, or weeks.

The term carrier means that an individual carries a pathogen in the body without showing any signs and symptoms of infection (asymptomatic infection or subclinical infection) but shed the pathogen and become a source of infection to other.

Advantages of Normal flora

1. **Prevent infection by either occupying receptors or producing harmful substances like bacteriocins that inhibit growth of pathogenic bacteria**

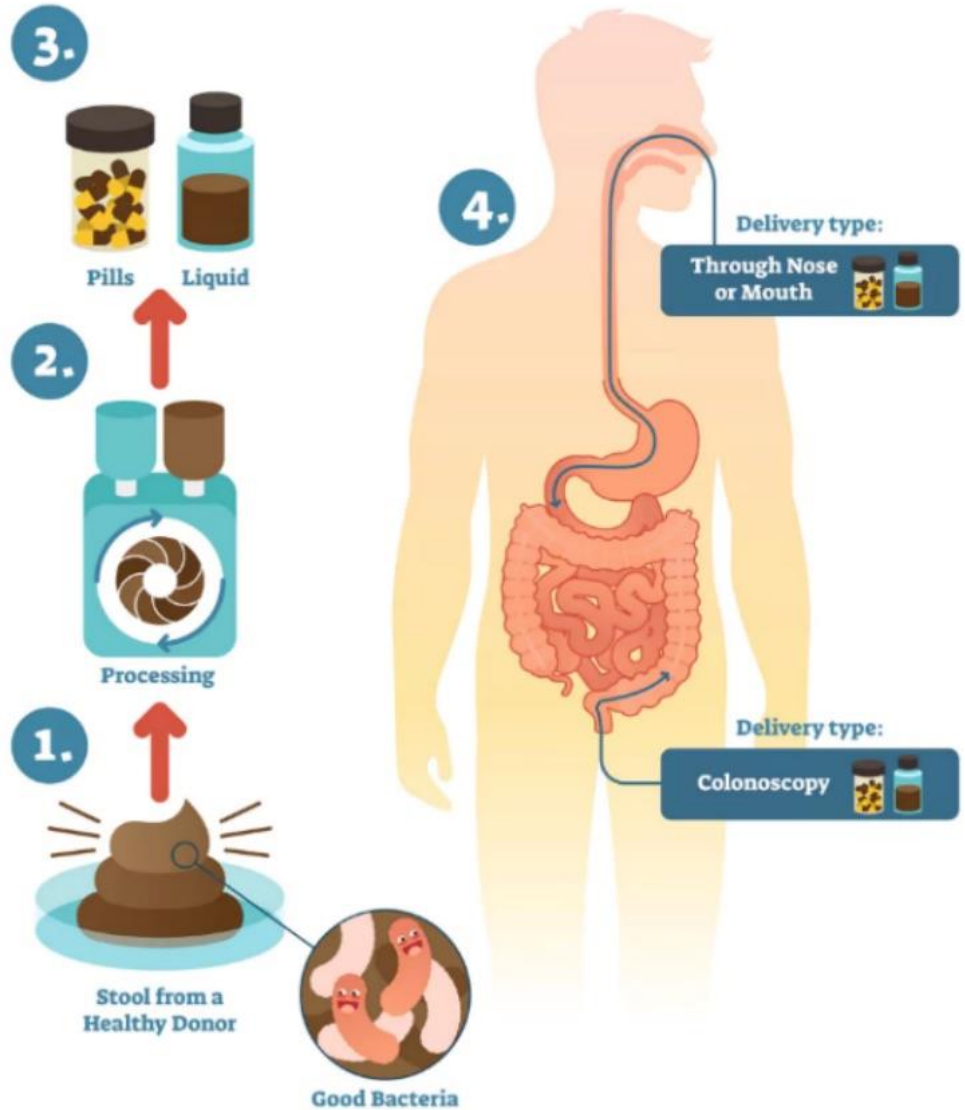
2. Participate in food metabolism in the gut and synthesis of Vit.K and B.

3. Stimulation of the immune system (mucosal immunity) . More than 80% our immune system is concentrated around GIT.

4. Source of probiotics (selected among normal flora)

5. Fecal microbiota transplantation for treatment of refractory cases of severe pseudomembranous colitis

FECAL TRANSPLANT THERAPY



Disadvantages of Normal flora

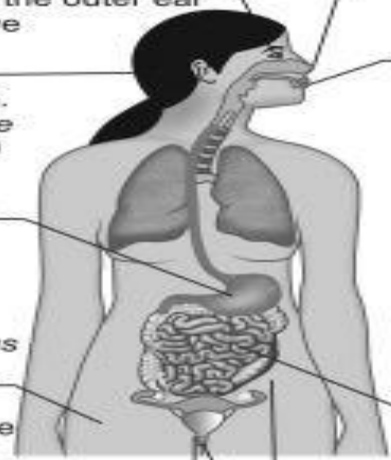
1.Opportunistic infections (Oral candidiasis in AIDS patients)

2. Antibiotic associated diarrhea like Pseudomembranous colitis caused by Clostridium difficile.

3. Penetrating trauma during abdominal surgery leads to leakage of intestinal contents into peritoneum and can cause peritonitis.

4. Tissue invasion like UTI in females by E.coli that come from GIT and dental caries caused by oral Strep.mutans.

5. Responsible for mixed growth when samples are taken from body area inhabited by normal flora



Normal microbiota of the conjunctiva
1. Coagulase-nagative *Staphylococci*
2. *Haemophilus* spp.
3. *Staphylococcus aureus*
4. *Streptococci* (various species)

Normal microbiota of the outer ear
1. Coagulase-nagative *Staphylococci*
2. *Diphtheroids*
3. *Pseudomonas* spp.
4. *Enterobacteriaceae (Peptostreptococcus)*

Normal microbiota of the stomach
1. *Streptococcus*
2. *Staphylococcus*
3. *Lactobacillus*
4. *Peptostreptococcus*

Normal microbiota of the skin
1. Coagulase-nagative *Staphylococci*
2. *Diphtheroids* (including *Propionibacterium acnes*)
3. *Staphylococcus aureus*
4. *Streptococci* (various species)
5. *Bacillus* spp.
6. *Malassezia furfur*
7. *Candida* spp.
8. *Mycobacterium* spp. (occasionally)

Normal microbiota of the urethra
1. Coagulase-nagative *Staphylococci*
2. *Diphtheroids*
3. *Streptococci* (various species)
4. *Mycobacterium* spp.
5. *Bacteroides* spp. and *Fusobacterium* spp.
6. *Peptostreptococcus* spp.

Normal microbiota of the vagina
1. *Lactobacillus* spp.
2. *Peptostreptococcus* spp.
3. *Diphtheroids*
4. *Streptococci* (various)
5. *Clostridium* spp.
6. *Bacteroides* spp.
7. *Candida* spp.
8. *Gardnerella vaginalis*

Normal microbiota of the nose
1. Coagulase-negative *Staphylococci*
2. *Viridans streptococci*
3. *Staphylococcus aureus*
4. *Neisseria* spp.
5. *Haemophilus* spp.
6. *Streptococcus pneumoniae*

Normal microbiota of the mouth and oropharynx
1. *Viridians streptococci*
2. Coagulase-negative *Staphylococci*
3. *Veillonella* spp.
4. *Fusobacterium* spp.
5. *Treponema* spp.
6. *Porphyromonas* spp. and *Prevotella* spp.
7. *Neisseria* spp. and *Branhamella catarrhalis*
8. *Streptococcus pneumoniae*
9. Beta-hemolytic *Streptococci* (not group A)
10. *Candida* spp.
11. *Haemophilus* spp.
12. *Diphtheroids*
13. *Actinomyces* spp.
14. *Ekenella corrodens*
15. *Staphylococcus aureus*

Normal microbiota of the small intestine
1. *Lactobacillus* spp.
2. *Bacteroides* spp.
3. *Clostridium* spp.
4. *Mycobacterium* spp.
5. *Enterococci*
6. *Enterobacteriaceae*

Normal microbiota of the large intestine
1. *Bacteroides* spp.
2. *Fusobacterium* spp.
3. *Clostridium* spp.
4. *Peptostreptococcus* spp.
5. *Escherichia coli*
6. *Klebsiella* spp.
7. *Proteus* spp.
8. *Lactobacillus* spp.
9. *Enterococci*
10. *Streptococci* (various species)
11. *Pseudomonas* spp.
12. *Acinetobacter* spp.
13. Coagulase-negative *Staphylococci*
14. *Staphylococcus aureus*
15. *Mycobacterium* spp.
16. *Actinomyces* spp.

Distribution of normal flora

- In every body site inhabited by normal flora there are a mixture of different kinds of bacteria but there is a predominant normal flora.

Skin

***Staphylococcus epidermidis* (predominant normal flora)**

Staphylococcus aureus (in small numbers) found in nasal cavity of 10-35% people.

Micrococcus species, α-Hemolytic and nonhemolytic streptococci (eg, *Streptococcus mitis*)

The predominant normal flora are aerobic and anaerobic *diphtheroid bacilli such as Corynebacterium* species and *Propionibacterium* species (hair follicles, sebaceous glands and sweat glands)

Peptostreptococcus species

Acinetobacter species

Small numbers of other organisms (*Candida* species in the skin folds), *Pseudomonas aeruginosa*, etc).

Non-pathogenic species of Mycobacterium occur in area rich of sebaceous secretions like genitalia and external ear. **(Make confusion with cases of renal T.B !!!!!!)**

- **Nasopharynx**
- Any amount of the following: diphtheroids, nonpathogenic ***Neisseria*** **species**, **α-hemolytic streptococci** **(viridans Streptococci= predominant)**; *S epidermidis*, non-hemolytic streptococci,
- anaerobes (too many species to list; varying amounts of *Prevotella* species, anaerobic cocci, *Fusobacterium* species, etc)
- Lesser amounts of the following when accompanied by organisms listed above: yeasts, *Haemophilus* species, pneumococci, ***S aureus***, gram negative rods, *Neisseria meningitides*

Mouth

Like nasopharynx

- **Gastrointestinal tract and rectum**
- Various Enterobacteriaceae except *Salmonella*, *Shigella*, *Yersinia*, *Vibrio*, and *Campylobacter* species. Glucose non-fermenting gram-negative rods
- Enterococci. α-Hemolytic and nonhemolytic streptococci
- Diphtheroids. *Staphylococcus aureus* in small numbers. Yeasts in small numbers
- Anaerobes in large numbers (too many species to list) **(the predominant normal flora is Bacteroides-anaerobes 10^{11}/gram of intestinal content, while the predominant facultative anaerobic bacteria is E.coli = 10^{8} /g of stool)**

- **Genitalia**
- Any amount of the following: *Corynebacterium* species, ***Lactobacillus*** **species (predominant)**, **α-hemolytic and nonhemolytic streptococci**, **nonpathogenic *Neisseria* species**
- The following when mixed and not predominant: enterococci, Enterobacteriaceae and other gram-negative rods, *Staphylococcus epidermidis*, *Candida albicans*, and other yeasts
- Anaerobes (too many to list); the following may be important when in pure growth or clearly predominant: *Prevotella*, *Clostridium*, and *Peptostreptococcus* species.

So in the vagina the predominant normal flora is a good bacteria called **lactobacilli** and another bad bacteria which are anaerobic bacteria one of them is ***Gardrenella vaginalis***. Under normal conditions there is a balance between these two normal flora but when it disturbs, much more anaerobic bacteria will grow and produce a condition called **bacterial vaginosis** which characterized by vaginal discharge with fishy odor and burning.

Urethra

The anterior urethras of both sexes contain small numbers of the same types of organisms found on the skin and perineum. These organisms regularly appear in normal voided urine in numbers of 10^2–10^4/mL (significant bacteriuria is 10^5/ml. and 10^4/ml in children).Therefore, first urine should be voided to wash out normal flora and mid-stream early morning urine is preferred for culture and sensitivity test.

So the best treatment of disturbed normal flora (Dysbiosis) is using probiotics

- **Definition**
- **Probiotics** are Live micro-organisms which when administered in adequate amounts confer a health benefit on the host (FAO/WHO 2002).
- **Prebiotics** are non- digestible food ingredients favor the growth of beneficial normal flora e.g fructo-oligosaccharide and inulin (1995).
- **Symbiotic= Probiotics + Prebiotics**

Do you know?

Total human cells= 10^{13}

Total human normal flora= 10^{14}

70% of normal flora is in colon

10^{11}bacteria/gram of colon content

>1000 bacterial species and only 50% had been isolated

80% of our immunity is concentrated around GIT.

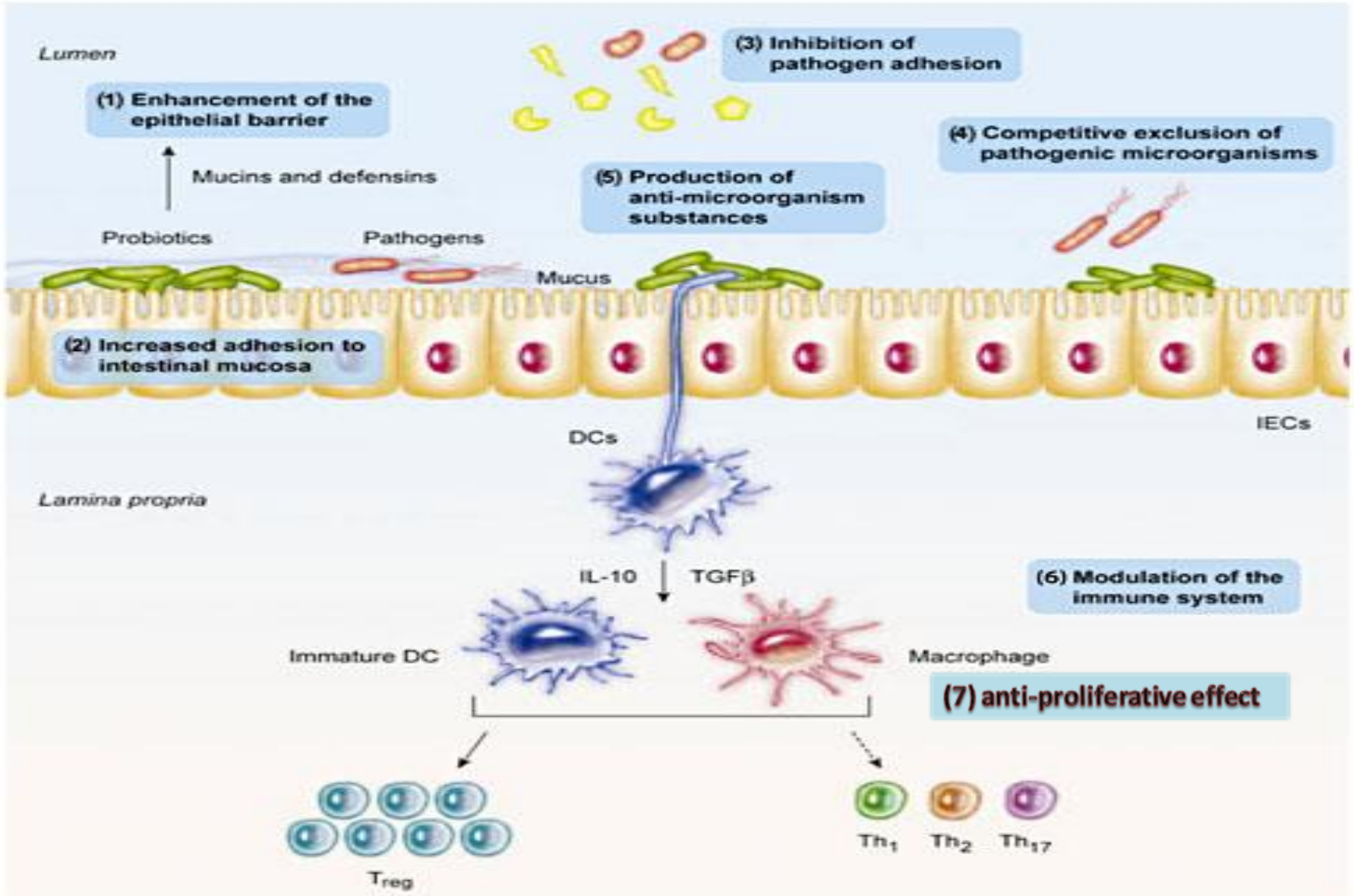
10^{3} - 10^{6}bacteria / teeth.

10^{7}bacteria /ml of the saliva

10^{4} -10^{5}bacteria/ml of vaginal fluid.

Total human genes=23000 while those of gut microflora= 3.3 million genes

Mechanisms of action



PROBIOTICS

LAB

- *Lactobacillus sp.*
- *Bifidobacterium sp.*
- *Enterococcus faecalis*
- *Enterococcus feacium*
- *Lactococcus lactis*
- *Leuconostic mesentroides*
- *Streptococcus thermophilus*

Non-LAB

- **Bacillus cereus*
- **E.coli* strain Nissle
- **Propionibacterium freudenreichii*
- **Saccharomyces cerevisiae*
- **Saccharomyces boulardii*

Criteria for Probiotics

- Human origin
- Nan pathogenic and non toxigenic
- Resistance to gastric acidity and bile toxicity
- Ability to colonize gut epithelial tissue
- Ability to persist within the G.I.T.
- Production of antimicrobial substances
- Ability to modulate immune response
- Resistance to antibiotics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16 PROBIOTIC STRAINS
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30 VEGETARIAN CAPSULES
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UP TO 60 SERVES
Baby Probiotic Broad Spectrum 2g
✓ 11 billion CFUs per sachet
✓ 10 natural probiotic strains
✓ Gentle digestive support
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AUSTRALIAN SINCE 1938 VITAMINS
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PROBIOTICS
CHEW ON THIS™
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DIETARY SUPPLEMENT 30 CHEWABLE TABLETS
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10 BILLION CFU + 6 STRAINS


TOSKANI
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PROBIOTICS ON
THE SKIN


#1 MOST STUDIED STRAIN†
RenewLife
Ultimate Flora™
WOMEN'S VAGINAL PROBIOTIC
Helps maintain healthy vaginal bacteria & yeast levels*
Supports urinary, digestive & immune health*
50 billion live cultures
12 probiotic strains
30 VEGETARIAN CAPSULES
PROBIOTIC SUPPLEMENT
NON GMO Project VERIFIED

Case # 1 related to lecture # 1

A 5- year- old boy suffered from bacterial infection of the lung (pneumonia). Ampicillin was prescribed for him to be taken by oral. After two days of treatment, the patient developed severe diarrhea and the physician prescribed anti candida drug like nystatin.

What you need to understand this problem?

1. A background on antimicrobial drugs
2. Normal flora especially intestinal normal flora
3. Probiotics

Questions

1. Why the patient developed diarrhea after taking ampicillin?
2. Why the doctor should give the patient anti candida drugs?
3. How to prevent such complication without prescribing antifungal drugs

Test yourself

Define 1- Normal flora,2- Probiotics, 3- Prebiotics, 4- Symbiotics, 5- opportunistic bacteria

1- What is the source of GIT normal of human of normally delivered baby?

2- Why surgeons should wash their hands before surgical operation and wear hand gloves with facial masks during operation?

3- Hand washing effect on which kind of skin normal flora?

4- How to know that the growth on blood agar from urine samples is due to contamination?

5- How to know that the growth of bacteria is coming from the sample of urine or from the contamination? Like Pseudomonas aeruginosa and Proteus sp. Because both of them widespread in the environment as saprophytic bacteria?

6- Why probiotic should be given after one hour from taking antibiotics orally?

7- How to increase the number of normal flora in your GIT?

8- Which kinds of home made food are rich of friend bacteria?