

Microbes and man

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Microbes and Man

- In uterus the child is sterile
- Colonization occurs during birth and in contacts thereafter; in adults 1,5 kg bacteria mainly in the gut
- Colonization during the first weeks/months adjusts development of microbiota and immunity
- "Human being is a walking culture medium for bacteria"

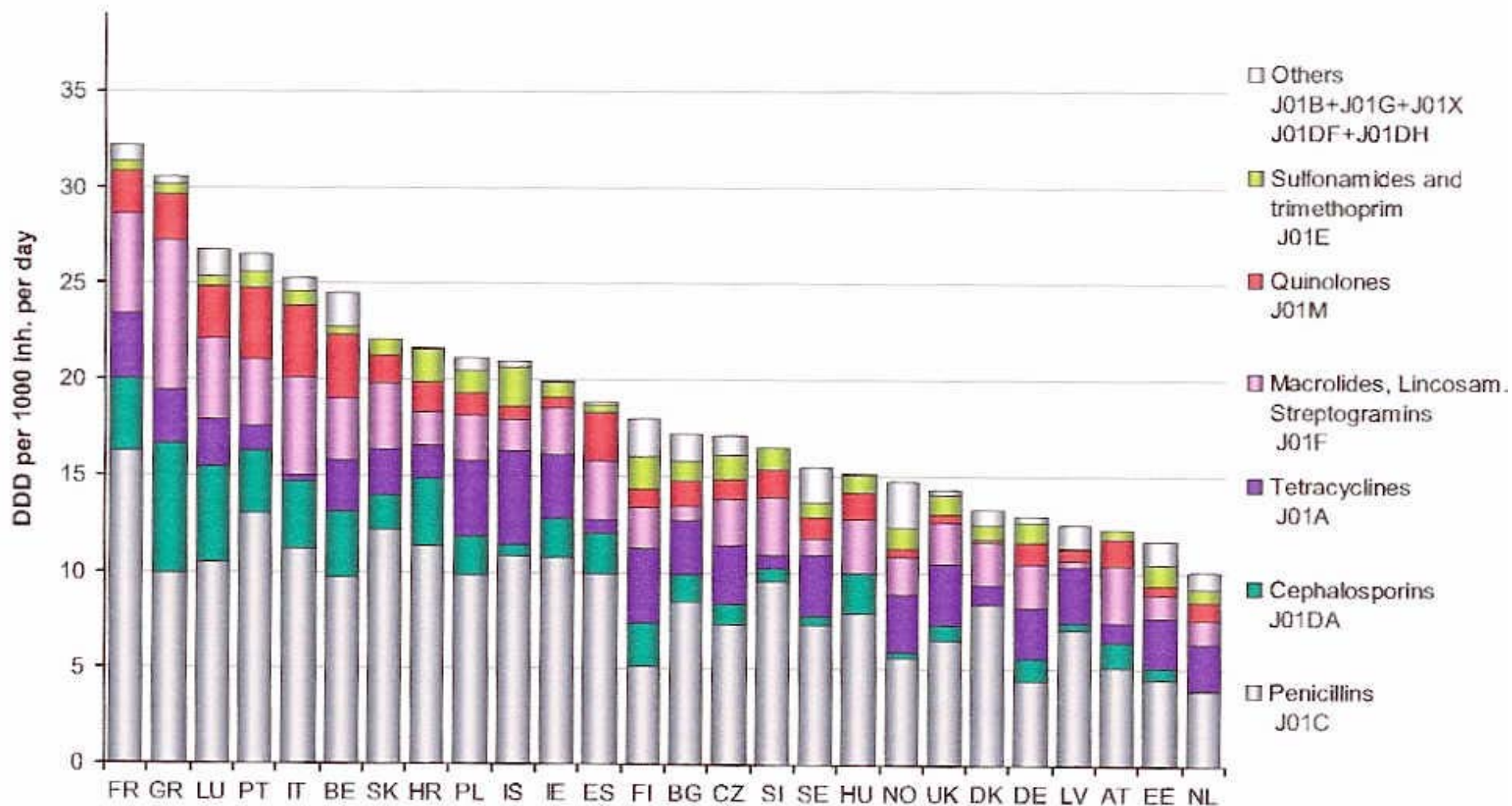
Human use of antibiotics

- Annual total production of antibiotics
 - in 1980 in USA 15 700 tons; 40% for animals
 - worldwide abt 40 000 tons/yr; during 30 yrs -> 1,2 million tons
- In Europe, national antibiotic use was published in June 2001
 - Cars O et al. Lancet 2001;357:1850-1852

Antibiotics and resistance

- Doctor
- Patients
- Bacteria
- Microbiota

Figure 1 Total outpatient antibiotic use in 26 European countries in 2002



Role of antimicrobial treatment

- ”In mice, which have been treated with streptomycin, the infective dose of exogenous microorganisms is between 1000 – 100 000 –fold lower than that in untreated mice.”
 - Vollaard EG, Clasener HAL. Antimicrob Agents Chemother 1994;38:409-14.
- Antimicrobial treatment is the worst incident that can meet human microflora

Allergy and bacteria

- Exposure to environmental bacterial endotoxin prevents allergy
 - Braun-Fahrlander et al. NEJM 2002;347:869-77
- Use of antibiotics and allergy in mice
 - Use of antibiotics destroys colonic microbiota and increases allergic response to *Aspergillus fumigatus*
 - Noverr et al. Infect Immun 2004;72:4996-5003 and 2005;73:30-8
 - Is bacteriotherapy a solution?

Gut bacteria produce enterolactone

- Enterolactone is a health promoting substance
 - hormonal active; produced by gut bacteria from e.g. vegetables, rye or linseeds
- Men with higher enterolactone serum concentrations had lower risk for acute coronary events
 - Vanharanta et al. Lancet 1999;354:2112-5; Arch Intern Med 2003;163:1099-104
 - ”These results add to the evidence supporting the importance of whole grain foods, fruits, and vegetables in the prevention of premature death from cardiovascular diseases.”

Enterolactone and antibiotics

- Women < 50 yrs and history of chronic UTI treatments have 74% higher risk for breast cancer
 - Knekt et al. Br J Cancer 2000;82;1107-10
- Women with more than 500 antibiotic treatment days have more than 2 times higher risk for breast cancer
 - Velicer et al. JAMA 2004;291:827-35
- Antimicrobial agents decrease serum enterolactone levels for 12-16 months
 - Effect continues up to 12-16 months
 - Kilkkinen et al. Am J Epidemiol 2002;155:472-7

Bacteriotherapy

- Bacteriotherapy has been given earlier in recurrent furunculosis and *C.difficile* diarrhoeae
 - Sanders WE, Sanders C. New Dimesions in Antimicrobial Therapy 1984
 - Tvede M, Rask-Madsen J. Bacteriotherapy for chronic relapsing Clostridium difficile diarrhoea in six patients. Lancet 1989;i:1156-60
- Broilact: prevention of salmonella in chickens
 - Nurmi E, Rantala M. Nature 1973;241:210-1.

Microbetherapy in gut disorders

- Lactobacillus GG capsules in antibiotic associated diarrhea
 - Arvola et al. Pediatrics 1999;104:e64
- Saccharomyces boulardii (Precosa^R) in C.difficile diarrhea
 - McFarland et al JAMA 1994;271:1913-8.
- E.coli ja mesalazine in the treatment of ulcerative colitis
 - Rembacken et al. Lancet 1999;354:635-9
- Trichuris suis worm therapy in Crohn's disease
 - Summers et al. Gut 2005;54:87-90

Gut microbiota and obesity

- Mouse gut microbiota given to germ-free mice led to 50% increase in fat tissue weight within two weeks even with a 30% reduction in the energy content of the diet
 - Bäckhed ym. PNAS 2004;101:15718-23
- Eckburg PB et al. Diversity of the human intestinal microbial flora.
Science 2005;science 1110592

Revolution ahead

- Only small part of microbes are known
- USA: The Microbe Project
 - 300-400 million USD; National Science and Technology Council (www.ostp.gov/html/microbial/start.htm)
- Bioterrorism act: DARPA 7,5 billion USD in 2005
- Next years will be more interesting than ever