The Dark Side of Antibiotics

Prof. Martin J. Blaser, MD
New York University School of Medicine

Wednesday, February 7, 2018
11:30am to 1:00pm
Mississippi Room, Coffman Union

consortium.umn.edu
The dark side of antibiotics

Martin J Blaser

Departments of Medicine and Microbiology
New York University School of Medicine
Department of Biology, NYU
Reflux Disease (GERD)

Diseases increasing in recent decades

Juvenile (type 1) diabetes

Sources:
Ann NY Acad Sci 2008 12:1150
Gut 1997;41:594
Obesity trends in US adults: changing physiology

Source: CDC Behavioral Risk Factor Surveillance System
Percent of adults who are obese, in 10 countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>33</td>
</tr>
<tr>
<td>UK</td>
<td>26.9</td>
</tr>
<tr>
<td>Australia</td>
<td>26.8</td>
</tr>
<tr>
<td>Russia</td>
<td>26.5</td>
</tr>
<tr>
<td>Germany</td>
<td>25.1</td>
</tr>
<tr>
<td>Spain</td>
<td>26.6</td>
</tr>
<tr>
<td>Mexico</td>
<td>32.1</td>
</tr>
<tr>
<td>Argentina</td>
<td>29.7</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>33</td>
</tr>
<tr>
<td>South Africa</td>
<td>31.3</td>
</tr>
</tbody>
</table>
Obesity trends among U.S. children and adolescents

Sex- and age-specific BMI > 95th %ile, based on CDC growth charts
Comparison of time trends of overweight & obese children globally

Prevalence: (>2SD above weight-for-height median) in children 0-5 years old

M de Onis et al. *Am J Clin Nutrition* 2010; 92; 1257-64.
Global number of overweight & obese children <5, by locale

Number of overweight and obese children (millions)

Number: (>2SD from weight-for-height median) in children 0-5 years old

M de Onis et al. *Am J Clin Nutrition* 2010; 92; 1257-64.
Worldwide trends in IBD incidence over 150 years

Concept 1: Evolution

Evolutionary relationships of wild hominids

H. Ochman et al. PLoS Biology 2010
Concept 2: Equilibrium

Schematic of interactions between a co-evolved colonizing microbe and host

Nature 2007; 449:843-9
What happens to the physiology of the host when the co-evolved microbe is lost (becomes extinct)?

- Robust
- Resilient

EMBO Reports 2006; Nature Rev Microbiol 2009
Concept 3: Age Window

When does the adult gut microbiome become established?

T Yatsunenko et al. Nature 2012;486, 222-7
Mother ➔ Child Transfer of Microbes (Ancient)

Mother → Child Transfer of Microbes (Modern)

Maternal exposures
- Antiseptics
- Antibiotics
- Dietary antibacterials

Bottle feeding

Extensive bathing

Antibiotics
Caesarean section

Changed human ecology has altered transmission and maintenance of ancestral microbes, which affects the composition of the microbiota. Especially important are microbes usually acquired \textbf{early in life}, since they affect a developmentally critical stage.

The effect of maternal status on the resident microbiota of the next generation

Prevalence of *Helicobacter pylori* in Japanese families

Approximate year of birth

- Grandmothers (244/355) -
- Mothers (251/578) 37%
- Children (101/808) 71%

% positive

Time (years)

0 20 40 60 80

Representation of a conserved microbiota

100%

Adapted from Y. Urita et al. *J Ped Child Health* 2013; 49:394-8
Antibiotics: one of the greatest discoveries of the 20th century

- Saved lives
- Revolutionized medicine

St. Mary’s Hospital, Paddington
• >73 billion antibiotic doses worldwide yearly
• USA (2010): 258 million courses (833/1000)
• Children: 2.7 courses by 2 years; 10.9 by 10 years
• Pregnancy: >50% treated or given prophylaxis

+ Exposures from use of antibiotics on the farm (scale unknown)
Variation in antibiotic use
Per capita antibiotic use in 31 countries in Europe

- Penicillins (J01C)
- Cephalosporins and other beta-lactams (J01D)
- Tetracyclines (J01A)
- Macrolides, lincosamides and streptogramins (J01F)
- Quinolones (J01M)
- Sulfonamides and trimethoprim (J01E)
- Other J01 classes

Cyprus, Greece, Lithuania: total use, including the hospital sector.
Spain: reimbursement data, does not include over-the-counter sales without prescription.
Malta: 2007 displayed.
Variation in antibiotic prescribing in the first year in life in 839 children in five European countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Median number of illness episodes</th>
<th>% of episodes treated with antibiotics</th>
<th>Prescription rate per infant per year</th>
<th>% of infants receiving ≥ 1 course of antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>3</td>
<td>18.4</td>
<td>1.3</td>
<td>55</td>
</tr>
<tr>
<td>Netherlands</td>
<td>3</td>
<td>9.8</td>
<td>0.6</td>
<td>37</td>
</tr>
<tr>
<td>Austria</td>
<td>4</td>
<td>6.7</td>
<td>0.5</td>
<td>33</td>
</tr>
<tr>
<td>Switzerland</td>
<td>4</td>
<td>3.9</td>
<td>0.2</td>
<td>18</td>
</tr>
<tr>
<td>Germany</td>
<td>4</td>
<td>5.1</td>
<td>0.5</td>
<td>33</td>
</tr>
</tbody>
</table>

Incidence of antibiotic use in the first 2 years of life by study site among 2134 children in the MAL-ED birth cohort, 2009-14

Rates of antibiotic prescribing for sick children

Excluding: preventive visits, CCC (Chronic Complex Conditions)
Standardized by: age, sex, age-sex, race, Medicaid status

JS Gerber et al. *J Pediatric Infect Dis* 2015
Rates of prescribing broad-spectrum antibiotics

Excluding: preventive visits, CCC, antibiotic allergy, prior antibiotics
Standardized by: age, sex, age-sex, race, Medicaid status
Trends in overall antibiotic prescribing for acute respiratory infections among USA Veterans, 2005-2012

BE Jones et al.
Ann Intern Med 2015
Variation in antibiotic prescribing for acute respiratory infections among USA Veterans, 2005-2012

Left. Variation among providers. The histogram shows the distribution of observed proportions of visits with an antibiotic prescription across 2594 providers with at least 100 ARI visits each (n= 480 875). The curve depicts the modeled distribution of antibiotic Rx’s across providers, after controls were set for the measured patient, provider, and setting.

Right. Sources of variation. The lines depict modeled distributions describing variation in proportion of antibiotic prescriptions attributable specifically to VAMCs, clinics, and providers, respectively, after controls were set for the measured patient, provider, and setting variables. The dashed-and-dotted line corresponds to the curve in the left panel and depicts overall modeled variation in antibiotic prescription across providers, including differences between providers at different clinics and VAMCs.
Outpatient antibiotic usage rates by region, 2010

Northeast
830

Midwest
868

West
638

South
936

National rate
833/1000 population
(258 million courses)

Sex-specific rates of antibiotic prescribing, 2011

<table>
<thead>
<tr>
<th>Sex</th>
<th>Prescriptions/1000 persons</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children (Age ≤ 19)</td>
<td>Adults (Age ≥ 20)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>941</td>
<td>990</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>841</td>
<td>596</td>
<td></td>
</tr>
</tbody>
</table>

LA Hicks et al. *Clin Infect Dis* 2015;60:1308-16
## Associations between county-level educational and income characteristics and high antibiotic prescribing

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Four-year college (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Lowest tertile (&lt;12.3)</td>
<td>1.0</td>
</tr>
<tr>
<td>Middle tertile (12.4-17.4)</td>
<td>0.9 (0.8-1.0)</td>
</tr>
<tr>
<td>Highest tertile (17.5-63.7)</td>
<td>0.6 (0.5-0.8)</td>
</tr>
<tr>
<td><strong>Per capita income ( x $1000)</strong></td>
<td></td>
</tr>
<tr>
<td>Lowest tertile (&lt;20.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Middle tertile (20.1-23.8)</td>
<td>0.8 (0.7-0.9)</td>
</tr>
<tr>
<td>Highest tertile (23.8-64.4)</td>
<td>0.5 (0.4-0.6)</td>
</tr>
</tbody>
</table>

\(a\) Defined as counties in the highest quartile of prescribing.

LA Hicks et al. *Clin Infect Dis* 2015;60:1308-16
Associations of antibiotic use with long term health consequences
Association between number of antibiotic purchases from birth to diagnosis of cow’s milk allergy in Finland

Adjusted model includes maternal age, smoking, prior deliveries, mode of delivery, and child’s birth weight.

Association between number of maternal antibiotic uses and risk of cow’s milk allergy in the offspring

Use of Antibiotics and Risk of Type 2 Diabetes: A Population-Based Case-Control Study

Kristian Hallundbæk Mikkelsen, Filip Krag Knop, Morten Frost, Jesper Hallas, and Anton Pottegård

Center for Diabetes Research (K.H.M., F.K.K.), Gentofte Hospital, University of Copenhagen, Hellerup; Novo Nordisk Foundation Center for Basic Metabolic Research (K.H.M., F.K.K.), Department of Biomedical Sciences, University of Copenhagen, Denmark; Department of Medicine (M.F.), Kolding Hospital, Kolding, Denmark; Endocrine Research Unit (M.F.), University of Southern Denmark, Odense, Denmark; and Clinical Pharmacology (J.H., A.P.), Department of Public Health, University of Southern Denmark, Odense, Denmark

Context and objective: Evidence that bacteria in the human gut may influence nutrient metabolism is accumulating. We investigated whether use of antibiotics influences the risk of developing type 2 diabetes and whether the effect can be attributed to specific types of antibiotics.

Methods: We conducted a population-based case-control study of incident type 2 diabetes cases in Denmark (population 5.6 million) between January 1, 2000, and December 31, 2012. Data from the Danish National Registry of Patients, the Danish National Prescription Registry, and the Danish Person Registry were combined.
Adjusted ORs for type 2 diabetes according to antibiotic exposure before initiation of diabetes treatment

<table>
<thead>
<tr>
<th>Type of Antibiotics</th>
<th>2-4</th>
<th>≥ 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any antibiotic</td>
<td><strong>1.21 (1.19-1.23)</strong></td>
<td><strong>1.53 (1.50-1.55)</strong></td>
</tr>
<tr>
<td>Narrow-spectrum</td>
<td>1.22 (1.20-1.23)</td>
<td>1.55 (1.53-1.57)</td>
</tr>
<tr>
<td>Broad-spectrum</td>
<td>1.18 (1.16-1.20)</td>
<td>1.31 (1.29-1.34)</td>
</tr>
<tr>
<td>Bactericidal</td>
<td>1.18 (1.17-1.20)</td>
<td>1.48 (1.46-1.50)</td>
</tr>
<tr>
<td>Bacteriostatic</td>
<td>1.20 (1.19-1.22)</td>
<td>1.39 (1.36-1.41)</td>
</tr>
</tbody>
</table>

ªOR for type 2 diabetes with redemption of 2-4 or ≥ 5 antibiotic prescriptions, compared with 0-1 redemptions.

KH Mikkelsen et al. *J Clin Endocrinol Metab* 2015
Ratio of antibiotic use in cases versus controls in the 15 years before initiation of treatment for T2D

Results are only for cases with an index between 2010 and 2012.

KH Mikkelson et al. *J Clin Endocrinol Metab* 2015
Outpatient antibiotic usage rates by region, 2010

Comparisons between the geography of obesity and antibiotic use, 2010

Is early life antibiotic exposure associated with increased weight gain?

Exposed to antibiotics during the first 6 months of life

* Significant difference in Z-score; p<0.05.


2011—2016: 16 studies published – 14/16 show parallel findings.
Antibiotics used in farm animals to promote their growth

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Class</th>
<th>Target</th>
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<tbody>
<tr>
<td>Bambermycin</td>
<td>Glycolipid</td>
<td>Cell wall</td>
</tr>
<tr>
<td>Virginiamycin</td>
<td>Streptogrammin</td>
<td>Protein synthesis</td>
</tr>
<tr>
<td>Avilamycin</td>
<td>Orthosomycin</td>
<td>Protein synthesis</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Cyclic peptide</td>
<td>Cell wall synthesis</td>
</tr>
<tr>
<td>Monensin</td>
<td>Ionophore</td>
<td>Cell membrane</td>
</tr>
<tr>
<td>Carbadox</td>
<td>Quinoxaline</td>
<td>DNA Synthesis</td>
</tr>
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(Adapted from Zimmerman, J Animal Sci, 1986)
Using mice to examine the effects of antibiotics

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<td>Quinoxaline</td>
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</tbody>
</table>

(Adapted from Zimmerman, J Animal Sci, 1986)
Body fat in antibiotic-exposed and control 10-week old mice

Control – 22.9% body fat

Antibiotic – 32.0% body fat

Effects of combining high fat diet and antibiotics

STAT = low-dose antibiotic exposure, as used on the farm

Laurie Cox
Cell 2014;158:705-21
HFD and antibiotic both contribute to body fat

<table>
<thead>
<tr>
<th></th>
<th>Control Normal Chow</th>
<th>High fat diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STAT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Amount of body fat**

**Male**

- Control-Normal Chow, n=8
- Control-High Fat Diet, n=9
- STAT-Normal Chow, n=10
- STAT-High Fat Diet, n=10

**Female**

- Lean Mass (g)

↑ High fat diet introduced

* p < 0.05 NC
° p < 0.05 HFD
DuraSTAT: Are changes **durable** with limited antibiotic exposure?

**Diet:**

- **Control**
  - Nursing 0-4 weeks: No antibiotics
  - Chow 4-6w: No antibiotics
  - High Fat Diet 6-28 weeks: No antibiotics

- **4-STAT**
  - Nursing 0-4 weeks: No antibiotics
  - Chow 4-6w: No antibiotics
  - High Fat Diet 6-28 weeks: No antibiotics

- **8-STAT**
  - Nursing 0-4 weeks: No antibiotics
  - Chow 4-6w: No antibiotics
  - High Fat Diet 6-28 weeks: No antibiotics

- **28-STAT**
  - Nursing 0-4 weeks: No antibiotics
  - Chow 4-6w: No antibiotics
  - High Fat Diet 6-28 weeks: No antibiotics

**Cell** 2014;158:705-21

Laurie Cox
Morphometric changes with limited antibiotic exposure

Diet:

- Nursing 0-4 weeks
- Chow 4-6w
- High Fat Diet 6-28 weeks

Control

4-STAT

8-STAT

28-STAT

Female C57

- Control n = 13
- 4-STAT n = 9
- 8-STAT n = 12
- 28-STAT n = 8

* P < 0.05, t-test

X₂: sacrificed 4 control and 4 8-STAT
X₃: sacrificed 3 control and 3 28-STAT
Effects of STAT on intestinal Th17 populations

Small intestine

Control | STAT
---|---
IL-17A | IL-22

Large intestine

Control | STAT
---|---
IL-17A | IL-22

*p<0.05 (t-test)

Jacqueline Leung
P’ng Loke Lab
Fecal community structure at 3 weeks

- **PC1 (9.2%)**
- **PC2 (6.7%)**
- **PC3 (4.8%)**

**Diet**
- **Milk**
- **NC**
- **HFD**

**Week**
- **Control**
- **4-STAT**
- **8-STAT**
- **28-STAT**

**Fat Mass (g)**

- **Control**
- **STAT**

*Graph showing differences in fat mass over weeks for different diets and groups.*
Is microbe-induced obesity transferable?

**Donors** → **Microbiota** → **Germ-Free recipients**

- **Control** (No abx)
- **Antibiotics** (No abx)

**Body composition - Days post-transfer**

**Total**

- Mass (g)
- Days: 0, 7, 14, 21, 28, 35
- Control vs. Antibiotics

**Lean**

- Mass (g)
- Days: 0, 7, 14, 21, 28, 35

**Fat**

- Mass (g)
- Days: 0, 7, 14, 21, 28, 35

*Significant differences*
Expression of genes involved in intestinal defenses in the microbiota of donor and recipient mice

**Th17**

- **RORγT**
- **IL-17A**
- **IL-17F**

**Antimicrobial peptides**

- **RegIIIγ**
- **β-Defensin**

p-values, by t-test
Effects of a single antibiotic pulse on microbial populations

Victoria Ruiz et al.
Nature Communications 2017
Effects of a single antibiotic pulse on host gene expression

How does the antibiotic pulse affect ileal gene expression in the mother and in her pups?
Ileal gene expression in PAT or control pups and dams

RNAseq analysis
Can microbiota transfer phenotypes across generations? A study of IBD
Microbiota communities until pup sacrifice at week 21

Unweighted UniFrac

PC1 (16%)

PC2 (9%)

PC3 (8%)
Transmission of taxa across generations

**Wildtype**

<table>
<thead>
<tr>
<th>Taxa (OTU):</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
</tr>
<tr>
<td>Dams</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>Pups</td>
</tr>
<tr>
<td>22 wPG</td>
</tr>
</tbody>
</table>

**IL10-/-**

<table>
<thead>
<tr>
<th>Taxa (OTU):</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
</tr>
<tr>
<td>Dams</td>
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<tr>
<td>2</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>Pups</td>
</tr>
<tr>
<td>22 wPG</td>
</tr>
</tbody>
</table>

---

**Authors:**

Serina Robinson  
Tonya Ward  
Dan Knights
Colonic pathology in IL-10-/- pups at week 21, according to the microbiota to which their mothers were exposed

Summary
Neither pups nor mother received antibiotics
Enhanced disease signal is entirely microbial
Antibiotic effect crosses generations
Inheritance also based on microbial genes
Antibiotic impact on long-term physiology through microbiota changes
Solutions
Antimicrobial use in USA farm animals, 2013

Medical Importance and Drug Class

- Medically Important³
- Not Currently Medically Important⁴

Annual Totals (kg)

- Aminoglycosides
- Cephalosporins¹
- Fluoroquinolones
- Lincosamides¹
- Macrolides
- Penicillins¹
- Sulfas¹
- Tetracyclines¹
- NIR²
- Ionophores
- NIR⁶

[^1]: Certain classes may include multiple specific drugs.
[^3]: Required by the FDA for human medical use.
[^4]: Not approved by the FDA for human medical use.
[^5]: A narrow spectrum of use.
[^6]: Not approved by the FDA.
## Antibiotic residues in food

<table>
<thead>
<tr>
<th>Source food</th>
<th>Antimicrobial agents in surveys</th>
<th>Concentration</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrimp</td>
<td>Fluoroquinolones</td>
<td>0.1-1.0 ng/g</td>
<td>USA</td>
</tr>
<tr>
<td>Salmon, trout, shrimp tissues</td>
<td>Fluoroquinolones</td>
<td>0.28-16 ng/g</td>
<td>Canada</td>
</tr>
<tr>
<td>Swine, chicken, shrimp tissues</td>
<td>Fluoroquinolones</td>
<td>1-100 ng/g</td>
<td>China</td>
</tr>
<tr>
<td>Bob veal, heavy calves, sows, heifers, market hogs, non-formula-fed veal,</td>
<td>Sulfonamides</td>
<td>0.1-1 ppm</td>
<td>USA</td>
</tr>
<tr>
<td>Bob veal, heavy calves, sows, heifers, market hogs, non-formula-fed veal,</td>
<td>Moxidectin (milbemycin)</td>
<td>89.13 ppb</td>
<td>USA</td>
</tr>
<tr>
<td>Bob veal, heavy calves, sows, heifers, market hogs, non-formula-fed veal,</td>
<td>Oxytetracycline</td>
<td>4.66 ppm</td>
<td>USA</td>
</tr>
<tr>
<td>Market hog, roaster pig meat</td>
<td>Carbadox</td>
<td>47-110 ppb</td>
<td>USA</td>
</tr>
<tr>
<td>Catfish, basa</td>
<td>Fluoroquinolones</td>
<td>1.9-6.5 ppb</td>
<td>China</td>
</tr>
<tr>
<td>Honey</td>
<td>Erythromycin</td>
<td>50-1776 ng/g</td>
<td>Turkey</td>
</tr>
<tr>
<td>Corn, green onion, cabbage</td>
<td>Chlortetracycline</td>
<td>2-17 ng/g</td>
<td>USA</td>
</tr>
</tbody>
</table>
Antibiotic Body Burden of Chinese School Children: A Multisite Biomonitoring-based Study

Hexing Wang,†,‡ Bin Wang,†,‡ Qi Zhao,† Yanping Zhao,‡ Chaowei Fu,† Xin Feng,§ Na Wang,† Meifang Su,¶ Chuanxi Tang,⊥ Feng Jiang,‡ Ying Zhou,*† Yue Chen,# and Qingwu Jiang†

†Key Laboratory of Public Health Safety of Ministry of Education, School of Public Health, Fudan University, Shanghai 200032, China
‡Minhang District Center for Disease Control and Prevention, Minhang District, Shanghai 201101, China
§Haimen City Center for Disease Control and Prevention, Haimen City, Jiangsu Province 226100, China
¶Yuhuan City Center for Disease Control and Prevention, Yuhuan County, Zhejiang Province 317600, China
⊥Changning District Center for Disease Control and Prevention, Changning District, Shanghai 200051, China
#School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario K1H8MS, Canada

Supporting Information

All 18 detected 58.3% of children were positive
Detection of antibiotics in urine by use category

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Human</td>
<td>4</td>
</tr>
<tr>
<td>B. Veterinary</td>
<td>3</td>
</tr>
<tr>
<td>C. Both</td>
<td>11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of courses taken</th>
<th>USA</th>
<th>Cumulative antibiotic use in the USA, by age</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2.73</td>
<td>2.73</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>8.17</td>
<td>10.90</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>6.78</td>
<td>17.68</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>13.38</td>
<td>31.06</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>19.93</td>
<td>50.98</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from L. Hicks *NEJM* 2013; 368:1461 (USA)
## Cumulative antibiotic use in the USA and Sweden

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of courses taken</th>
<th>USA</th>
<th>Sweden</th>
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<td></td>
<td>During period</td>
<td>Cumulative</td>
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<td>2.73</td>
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<td>-</td>
<td>1.39</td>
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<td>8.17</td>
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Adapted from L. Hicks *NEJM* 2013; 368: 1461 (USA)
A. Ternhag *NEJM* 2013; 369: 1175 (Sweden)
Diversity loss in the microbiome in 3 model locales

Science 2016
Next steps for the microbiome?

Science 2016
Medicine of the future: new analyses of child health

Analysis

Global microbes

Personal microbes

Host markers

• Genotype
• Biomarkers
New approach to optimize child health?

- Global microbes
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  - Genotype
  - Biomarkers

Administer

Analysis
New algorithm for preventing illnesses?

Analysis

Global microbes
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Administer

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Assess for positivity, phenotypes

Drug the microbiome