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## ***Antibiotics & Weight Gain In Humans***

In humans, many of the same biological mechanisms observed in animals are relevant—including microbiome remodeling, immune reactions, inflammatory shifts, bile acid signaling, and endocrine effects. However, in the real world the average effect is typically smaller and more variable than in livestock, because exposures are usually short, diets vary widely, and the reason for antibiotic use (illness) is an important confounder.

### **1) The Headline: Antibiotics Can Promote Weight Gain, but It's Context-Dependent**

- In animals antibiotics are often given continuously at low dose, with controlled diets and higher pathogen pressure—making the growth effect large and reproducible.
- In humans antibiotics are usually short courses; diets and pathogen exposure vary; and underlying illness confounds outcomes—so effects are often modest on average but more pronounced in specific contexts.

### **2) Strongest Real-World Human Signal: Early-Life Antibiotic Exposure**

Many cohort studies associate antibiotics in infancy/early childhood with:

- Higher BMI later
- Increased risk of overweight/obesity
- Sometimes a dose-response relationship (more courses → larger effect)

Why early life is different. Early childhood is a key window for:

- Microbiome establishment

- Immune tolerance formation
- Metabolic signaling development
- Likely dominant mechanisms:
  - Long-lasting microbiome shifts (lower diversity, altered taxa)
  - Immune programming and inflammation set points
  - Bile acid and SCFA signaling changes
  - Greater energy harvest from diet

### **3) Adults: Weight Gain Can Happen, but Often Indirectly**

In adults, the relationship is real but less predictable because adult microbiomes are more stable and the reasons antibiotics are prescribed vary widely.

Direct microbiome/metabolic effects (can occur):

- Short courses can still cause:
  - Decreased microbiome diversity
  - Blooms of opportunistic organisms
  - Altered bile acid conversion
  - Changed SCFA profiles
- Clinical patterns that may be seen:
  - Appetite changes
  - Altered satiety signaling
  - Transient water retention or GI changes
  - Mild fat gain in some individuals over weeks–months

Note: For many adults, but not all, partial microbiome recovery occurs over time.

“Sickness confounding” (very common):

- People receive antibiotics because they are sick, and illness itself affects weight—so observational data can reflect illness + behavior + microbiome effects. Examples:
  - Some infections cause weight loss, so recovery appears as weight gain
  - Inflammation, sleep disruption, inactivity, and dietary shifts can change weight
  - Repeated antibiotics may reflect underlying chronic conditions

#### **4) The Clearest Adult Scenario: Repeated or Prolonged Exposure**

- Stronger signals appear when:
  - Multiple courses occur per year
  - Broad-spectrum antibiotics are used repeatedly
  - Exposure spans months (e.g., recurrent infections or prophylaxis in some conditions)
- Why repeated courses matter:
  - Incomplete microbiome recovery between courses
  - Each course acts like another “reset”
  - Cumulative shifts can tilt energy harvest, signaling, and inflammation

#### **5) Translating Animal Mechanisms to Humans (Mechanism-by-Mechanism)**

- Mechanism 1: More calories harvested
  - Humans may absorb more energy from the same diet if microbiome shifts favor fermentation efficiency.
  - The effect varies with diet; higher fiber provides more substrate for microbial fermentation.
- Mechanism 2: Lower immune activation
  - If antibiotics reduce chronic low-grade pathogen load, inflammation may drop and metabolic efficiency may improve.
  - However, dysbiosis can sometimes increase inflammation later depending on the microbial replacement pattern.
- Mechanism 3: Improved absorption
  - Reducing gut inflammation and diarrhea can improve nutrient absorption.
  - This may be more noticeable in individuals with chronic GI issues.
- Mechanism 4: Reduced microbial competition
  - Likely less important in well-nourished adults but potentially relevant in infants or undernutrition.
- Mechanism 5: Bile acid signaling

- Highly plausible in humans: antibiotics can alter bile acid pools and FXR/TGR5 signaling.
- This can influence fat storage, glucose metabolism, and appetite regulation.
- Mechanism 6: Reduced growth-suppressing metabolites
  - May help in certain GI states (e.g., reducing toxin-producing bacteria) but can also increase risks such as *C. difficile* depending on context.
- Mechanism 7: Appetite and endocrine effects
  - Microbes influence GLP-1, PYY, and ghrelin; antibiotic shifts may alter appetite and satiety.
  - Some people experience appetite increases; others have reduced appetite.
- Mechanism 8: Reduced subclinical disease pressure
  - Translates best when a person has ongoing low-level infections or inflammation.
  - Eliminating pathogens is not always a pure win; outcomes depend on microbial replacement.

## **6) Important Counterpoint: Antibiotics Can Increase Metabolic Risk Without “Healthy” Weight Gain**

In livestock, weight gain is economically beneficial and interpreted as improved growth. In humans, antibiotic-associated weight gain may reflect increased fat deposition or altered insulin sensitivity, so the concern is less “growth promotion” and more obesity and metabolic risk—especially with early-life exposure.

## **7) Practical Meaning (The “So What?”)**

- If someone asks, “Will antibiotics make me gain weight?”
  - A single short course: usually minimal lasting effect, though appetite/GI changes can occur.
  - Repeated or early-life exposure: stronger association with weight gain risk.
  - The largest and most consistent human signal is early childhood, not occasional adult use.
- What happens after antibiotics matters most:
  - Diet quality and fiber intake (supports microbiome recovery)
  - Avoiding unnecessary repeat courses

- Recovery of microbiome diversity
- Baseline metabolic risk profile