Absorption of Toxicants

Food Toxicology
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Learning Objectives

- Describe the ways in which toxicants interact with cells.
- Recognize how the molecular characteristics of toxicants affect entrance into a cell.
- Explain human anatomy as related to integumentary, respiratory and digestive systems.
- Summarize the routes of toxicant absorption.

Organization of the Body

Metabolism: Molecular Organization

Biosynthesis/Catabolism (Enzymes, ATP)

<table>
<thead>
<tr>
<th>MONOMERS</th>
<th>POLYMERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>subunits</td>
<td>macromolecules</td>
</tr>
<tr>
<td>saccharides</td>
<td>polysaccharides</td>
</tr>
<tr>
<td>glucose</td>
<td>glycogen</td>
</tr>
<tr>
<td>amino acids</td>
<td>proteins</td>
</tr>
<tr>
<td>nucleotides</td>
<td>DNA, RNA</td>
</tr>
</tbody>
</table>

Composition of Bacteria

<table>
<thead>
<tr>
<th>Types of molecules</th>
<th>% of total weight</th>
<th>E. coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>70</td>
<td>1</td>
</tr>
<tr>
<td>Proteins</td>
<td>15</td>
<td>3000*</td>
</tr>
<tr>
<td>Nucleic Acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>RNA</td>
<td>6</td>
<td>&gt;3000*</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Lipids</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Building block molecules</td>
<td>2</td>
<td>500</td>
</tr>
<tr>
<td>Inorganic ions</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>
The Cell

- Replication
- Transcription
- Translation

DNA → RNA → Proteins

Nucleus → Ribosomes → Cytoplasm

Proteins

Proteins

- Synthesized primarily during a process called translation.
- Building blocks of proteins are amino acids.
- Proteins are made of a long chain of amino acids
  - Peptide bonds; disulfide bonds (Cys).
  - Primary structure is sequence.
- Sometimes modified by:
  - Heme, sugars, phosphates.

Amino Acids

- Ala
- Asp
- Cys
- Phe

Amino Acid Chains

α Helix Secondary Structure

Also:
- β - pleated sheet
- Random coil
Hemoglobin Protein Structure

Protein Functions
- Antibodies.
  - Recognize molecules of invading organisms.
- Receptors.
  - Part of the cell membrane; recognize other proteins, or chemicals, and inform the cell.
- Enzymes
  - Assemble or digest.
- Neurotransmitters, hormones
  - Trigger receptors.
- Channels and pores.

Cellular Absorption
- Diffusion.
  - Requires concentration gradient.
  - Fick's Law.
- Facilitated diffusion.
  - Membrane surface carrier proteins.
  - Glucose transport.
- Active transport.
  - Requires cellular energy (ATP).
  - Endo/exo-cytosis.
  - Phago/pino-cytosis.

Cell Membrane
- Phospholipid bilayer

Four Types of Cells
- Epithelia.
  - Coverings, linings, secretions.
- Connective.
  - Support, energy.
- Muscle.
  - Movement.
- Nervous.
  - Electrical impulse, information.

Epithelia
Food Toxicology

Nerve

Eleven Organ Systems

- Integumentary
- Skeletal
- Muscular
- Nervous
- Endocrine
- Cardiovascular
- Lymphatic
- Digestive
- Respiratory
- Urinary
- Reproductive

Absorption

- Process by which toxicants cross the epithelial cell barrier.

Routes of Absorption

- Integumentary (percutaneous).
- Respiratory.
- Digestive.

Integumentary System Route

- Skin, hair, nails, mammary glands.
  - Skin is the largest organ in the body.
- Epidermis.
  - Avascular, keratinized stratum corneum, 15-20 cells thick, provides most toxicant protection.
- Dermis.
  - Highly vascularized; nerve endings, hair follicles, sweat and oil glands.
- Hypodermis.
  - Connective and adipose tissue.

Skin

- Stratum corneum
- Stratum granulosum
- Stratum lucidum
- Stratum basale
- Epidermis
- Dermis
- Subcutaneous tissue
- Hair follicle
- Artery
- Vein
- Sweat gland

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Case Study: Skin Lesion

Kenyan Beetle Toxin

Some beetles have mixing chambers in their abdomens that produce a hot, violently exploding poison. This quinone based toxin can be directed at threats.

Bombardier beetles related to the genus Brachinus.

Respiratory System Route

- Skin: stratified squamous epithelial tissue.
- Respiratory system: squamous epithelium, ciliated columnar and cuboidal epithelium.
  - Non-keratinized, but ciliated tissues and mucus-secreting cells provide "mucociliary escalator".
- Nasopharyngeal.
- Tracheobronchial.
- Pulmonary.

Respiratory Tract

- Nasopharyngeal.
  - Nostrils, nasopharynx, oropharynx, laryngopharynx.
  - Hairs and mucus; trap >5 μm particulates.
- Tracheobronchial.
  - Trachea, bronchi, bronchioles; ciliary action.
  - Luminal mucus traps 2-5 μm particulates and H₂O soluble aerosols and gases.
- Pulmonary
  - Alveoli - high surface area gas exchange with cardiovascular system.

Lung Dissection

Bronchus-Bronchiole Dissection
Case Study: Fixed Obstructive Lung Disease in Workers at a Microwave Popcorn Factory

Missouri, 2000—2002

- In May 2000, an occupational medicine physician contacted the Missouri Department of Health and Senior Services (MoDHSS) to report eight cases of fixed obstructive lung disease in former workers of a microwave popcorn factory. Four of the patients were on lung transplant lists.
  - All eight had a respiratory illness resembling bronchiolitis obliterans (chronic scarring) with symptoms of cough and dyspnea on exertion, had worked at the same popcorn factory at some time during 1992–2000.

Morbidity and Mortality Weekly Report, April 26, 2002 / 51(16);345-7

Diacetyl Butter Flavor

- Industrial hygiene sampling conducted during the November 2000 survey detected approximately 100 VOCs in the plant air.
- Diacetyl, a ketone with butter-flavor characteristics, was measured as a marker for exposure to flavoring vapors. The geometric mean air concentration of diacetyl was 18 ppm in the room air where the mixing tank was located, 1.3 ppm in the microwave packaging area, and 0.02 ppm in other areas of the plant.
- Rates of obstructive abnormalities on spirometry increased with increasing cumulative exposure to airborne flavoring chemicals.

Digestive System Route

- Mouth, oral cavity, esophagus, stomach, small intestine, rectum, anus.
- Residence time can determine site of toxicant entry/injury.
  - Mouth (short); small intestine (long).
  - Absorption of toxicants can take place anywhere, but much of the tissue structure in the digestion system is specially designed for absorption.

Digestive System Route, 2

- Tissue differentiation.
- Mucosa
  - Avascular, s. squamus or columnar epithelium.
  - In some regions villi and microvilli structure aids in absorption (high surface area).
- Submucosa
  - Blood, lymph system interface.
- Muscularis (movement).
- Serosa (casing).
Jin Bu Huan Toxicity: Patient 1

- A 13-month old boy was lethargic and breathing abnormally when found by his mother approximately 20 minutes after he ingested approximately 60 Jin Bu Huan tablets. The child exhibited CNS depression and was responsive only to painful stimuli. In the emergency department, he was lethargic, with hypotonia, and transient bradycardia.
  - An extensive toxicologic screen was negative. He was treated with activated charcoal through an orogastric tube. He became more alert during the next 10 hours until his physical examination and mental status were completely normal. Follow-up indicated no permanent sequelae.

Jin Bu Huan Toxicity: Patient 2

- A 2 1/2-year-old girl was lethargic and breathing abnormally when found by her mother 30-60 minutes after she ingested approximately 17 Jin Bu Huan tablets. Paramedics found the child unresponsive with respiratory depression. An acute episode of bradycardia was successfully treated with atropine. Initial examination in the emergency department indicated miotic pupils, CNS depression, and a disconjugate gaze. The patient’s respiratory rate diminished, requiring intubation within 20 minutes after arrival to the emergency department. During the next hour, the child’s condition improved, and during an episode of vomiting, she extubated herself.
  - Gastrointestinal decontamination treatment included performing gastric lavage (resulting in recovery of pill fragments) and administering activated charcoal and a cathartic. She remained intermittently lethargic with diffuse muscle weakness until approximately 8 hours following ingestion. Urine and serum toxicologic screens were negative for more than 30 substances. She was discharged the following day after a complete recovery. Follow-up indicated no permanent sequelae.

Jin Bu Huan Toxicity: L-THP Alkaloid

- The tablets were 36% concentrated weight-by-weight levo-tetrahydro-palmatine (L-THP)
  - L-THP is present in the plant genus Stephania but not in the genus Polygala – the plant of origin indicated on the Jin Bu Huan product package insert.
  - Morphine-like properties.
- Each tablet contained 28.8 mg L-THP; no other plant alkaloids were present in tablets tested from multiple bottles of Jin Bu Huan.