Take as Directed

Pharmacokinetics and Contributing Physiologic Changes During Space Flight

Four decades of experience reveal that virtually every system in the body is affected by space flight—the digestive system is no exception. It plays two crucial roles: 1) digestion of food and water and 2) distribution of medicine. Any medication must be absorbed, processed, and then eliminated from the body by several digestive organs, including the stomach, intestines, liver, and kidneys. But the physiological changes accompanying space flight may change the effectiveness of oral medications taken by astronauts. To the astronaut experiencing space motion sickness, this could be an unpleasant prospect!

During flight, astronauts take medications for two reasons: routine medical care or countering certain effects of microgravity. Unlike clinicians on Earth who can examine patients in person, NASA physicians care for astronauts orbiting more than 200 miles above! Drugs are a practical option for treatment as they can be easily dispensed and administered in space. The most frequent reasons for using medication on orbit include space motion sickness (SMS), insomnia, congestion, and back pain—all relatively uncomplicated ailments that are easily treated on Earth with drugs.

Use of in-flight medication dates back to the Mercury era, when astronauts used anti-nausea drugs for SMS. A long list of medications is currently approved for all flights. On Earth, we assume that medications, whether prescribed or purchased over the counter, have maximum therapeutic effect and minimum side effects. For astronauts, taking a medication is far more complex because many factors encountered in flight may compromise the drug's effectiveness.

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Astronauts James Newman (left) and Daniel Bursch give breath samples on STS–51 to show the breakdown of test substances by bacteria in the GI system. This test will be performed before and after the STS–107 flight.

In this study of pharmacokinetics, scientists investigate the effect of microgravity on drug absorption and elimination and the function of specific body systems that affect drug disposition in space.

Earth Benefits and Applications

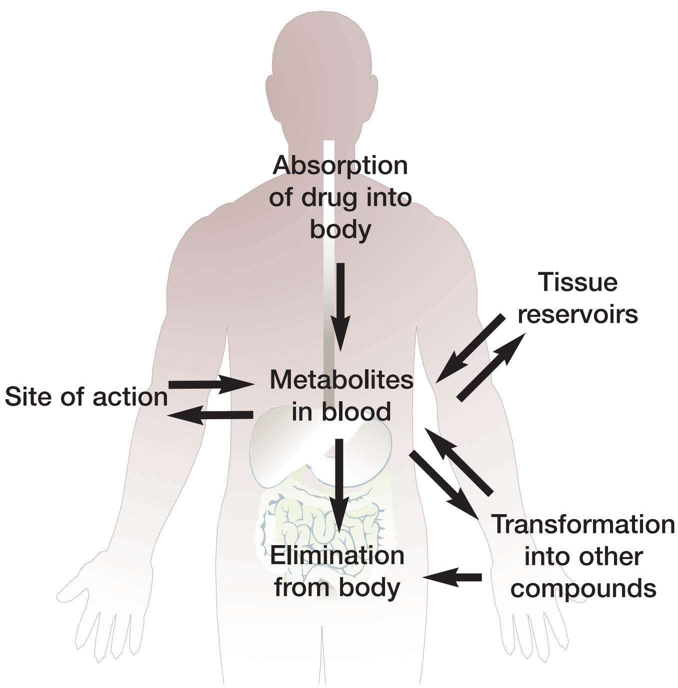
- Understand gastrointestinal disorders and diseases in adverse environmental conditions
- Improve delivery methods of medications for treatment
- Establish innovative, non-invasive ways to measure drug availability in the body
- Validate inexpensive ambient storage for biological samples.

Using non-invasive pharmaceutical probes (instead of invasive clinical techniques), scientists can examine the function of the gastrointestinal system (GI; the stomach and intestines), renal system (kidney), and hepatic system (the liver). This data will substantiate earlier observations and build on existing data, ultimately yielding more effective treatments in space.

Background Information

Science

To be effective, a drug must first be absorbed from the GI system into the bloodstream. There the metabolites, or the components of the drug after breakdown, are distributed throughout the body—including the location in the body where it is needed, known as the site of action. Simultaneously, the drug is also eliminated from the body by the liver and kidneys. Pharmacokinetics characterizes these processes, all of which determine drug concentration in the body and therefore, its overall effectiveness. The bioavailability of a drug, an important indicator of a drug's clinical effectiveness, refers to the quantity of drug that is available in the body after it has been taken.



This schematic shows the interrelationship between drug absorption, distribution, and elimination.

Data and reports collected over the past ten years suggest that the GI, renal, and hepatic systems are indeed affected by space flight, although these effects are not well characterized. Well-documented changes—such as altered distribution of body fluids and changes in the cardiovascular system (heart, blood vessels, and blood flow)—likely affect the other systems mentioned above, leading to changes in drug effectiveness in space. By studying pharmacokinetics before and after flight, scientists aim to understand drug dynamics in space, in addition to examining functional changes in important organ systems such as the GI tract and the liver. Drug levels in the body are valuable indicators of many parameters that characterize how these systems are affected by space flight.

Operations

The overall protocol includes three procedures, each carried out before and after space flight. Astronauts collect breath, saliva, and urine samples before they take any medication. They then ingest oral acetaminophen, a common over-the-counter pain reliever, and lactulose, a non-digestible sugar. Acetaminophen and lactulose act as pharmaceutical probes, which allow scientists to trace many GI parameters without using any invasive clinical tests. Saliva, breath, and urine samples are collected at timed intervals after the astronauts take the probes.

Next is a procedure to determine whether the GI environment changes as a result of space flight. Astronauts first ingest glucose and urea (with a special carbon molecule), then collect breath samples for measuring the release of certain gases. Glucose and urea are innocuous substances that also act as probes; their breakdown can be tracked in the body by measuring how much hydrogen and carbon dioxide are released in the breath as a result of bacterial activity. Under normal conditions, low levels of certain beneficial bacteria are present in the GI system, and thus no hydrogen or very little hydrogen is seen in the breath. A higher level of hydrogen in the breath after taking glucose indicates an increase in the bacterial colonies in the GI system.

The urea test indicates the levels of *Helicobacter pylori*, a slow-growing and harmful bacterium present in the stomach. The test measures the level of carbon dioxide, which features the special carbon molecule that can be easily tracked. Under normal, healthy conditions, *H. pylori* does not grow significantly and therefore does not pose a health risk.

These tests are repeated two times before flight and two times after space flight. By comparing the hydrogen and carbon dioxide levels before flight to levels after flight, scientists will be able to determine if space flight has an effect on the GI environment of astronauts.

Earlier Studies

This study for STS–107 is actually one in a series of ongoing pharmacokinetic studies. Because so few astronauts fly on each mission, subjects must be recruited from many missions to obtain enough data. A similar study was first conducted in 1993 on STS–51, a short-duration mission, and on *Mir*–18/STS–71, a long-duration mission. Based on the limited results from these flights, experimental methods have been modified for the present study to evaluate physiology of the GI system.